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Consulting reviewer:
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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. PROSPECTIVE STUDY OF FLEXIBLE RECTOSIGMOIDOSCOPY IN AN ASYMPTOMATIC POPULATION AS A SCREENING PROCEDURE FOR POLYPS.

Allemand H, Dreyfus T, Deschamps JP, Vuitton D, Carbillet JP, Miguet JP, Carayon P

Departement de Medecine Preventive, Sante Publique et Hygiene, Faculte de Medecine et de Pharmacie, F-25030 Besancon Cedex, France

Gastroenterol Clin Biol; 5(8/9):742-746 1981

The screening of 170 patients (92 men, 78 women; 40-75 yr old, mean age of 58.5 yr) hospitalized for nonintestinal symp-

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toms and with no history of intestinal polyps or cancer with flexible rectosigmoidoscopy (FR) is described. Only 1.7% refused the procedure. The mean duration of the examination was 6.7 min (4-14 min). The preparation of the colon was found to be adequate or perfect in 91% of the patients. The patient tolerance for FR was good in 94% of the patients. In 6% of the patients, injection of a spasmolytic agent was required. In five patients, it was necessary to halt the procedure. FR allowed the examination of a mean of 57.6 cm of the colon, with more than 55 cm examined in in 78% of the patients. In 18 subjects, 22 polyps were identified. Polyps were found in 12% of the men and 9% of the women. More than 2/3 of the polyps were situated outside of the range (20 cm) of rectosigmoidoscopy. The mean diameter of the polyps was 7.4 mm (3-25 mm). Of the polyps, 68.2% were adenomas (14 tubular and 1 tubulovillous) and 31.8% were hyperplastic or inflammatory polyps. The results indicated the efficiency of FR as a screening procedure for polyps. (14 Refs) (In FRE)

2. EARLY DETECTION OF COLORECTAL TUMORS IN HIGH-RISK GROUPS.

Rozen P, Fireman Z, Hellerstein SM, Rattan J, Gilat T
Gastroenterology Dept., Ichilov Hosp., Tel Aviv Univ., Tel Aviv, Israel
Harefuah; 100(5):214-216 1981

Early detection of colorectal cancer through a screening program which uses examination of stool for occult blood and/or flexible sigmoidoscopy or colonoscopy is described. In this pilot study 711 persons were examined: tumors were identified in 0.5% of control rural and urban populations, and in 3.8% and 61.3%, respectively, of high risk groups with a family history of colonic tumors and with a history of benign or successfully treated malignant colonic tumors. (19 Refs) (In HEB)

3. SHOULD COLORECTAL CARCINOMA BE SOUGHT IN PERIODIC HEALTH EXAMINATIONS? - AN APPROACH TO THE EVIDENCE.

Fletcher SW, Dauphinee WD
Box 105, North Carolina Memorial Hosp., Chapel Hill, NC, 27514
Clin Invest Med; 4(1):23-31 1981

The approach of the Canadian Task Force on the Periodic Health Examination for screening for colorectal carcinoma is reviewed. Three basic questions were involved in the study. First, how effective is early treatment for uncovered disease. Many cohort studies have suggested that surgical intervention before the spread of colorectal cancer gives superior results compared to similar treatment after spread, and that intervention in the presymptomatic phase of the disease is better than intervention when symptoms occur. The second question regards the burden of suffering that colorectal cancer causes afflicted persons and society in general. The available evidence indicates that colorectal cancer causes a substantial burden of suffering, and that this burden is primarily on the elderly. The third question is whether there is a good screening test for colorectal cancer. Most attention has been given sigmoidoscopy and testing the stool for occult blood. No single test has been found to be inexpensive, safe, simple, sen sitive, specific, and acceptable. Sigmoidoscopy is costly, often not acceptable, and not totally safe. Testing for occult blood in the stool (Hemoccult test) is safe and inexpensive, but often unacceptable. Further research is needed to develop a good test for early detection. In the meantime, testing for occult blood in the stool is recommended annually for persons over 45 yr of age. (67 Refs)

4. SCREENING FOR COLORECTAL TUMORS - RESULTS OF TWO YEARS EXPERIENCE.

Ribet A, Escourrou J, Frexinos J, Delpu J
Clinique des Maladies de l'Appareil Digestif, Centre Hospitalier Universitaire de Rangueil, 31054 Toulous cedex, France
Cancer Detect Prev; 3(2):449-461 1981

The experience after 2 yr of systematic colorectal tumors screening of 603 subjects, aged between 40 and 70, is reported. All subjects were submitted to proctoscopy (P) and air filled barium enema (AFBE). Total frequency of screened tumors: 15.25%. More than 85% of the tumors were found in the recto-sigmoid. Two subgroups were identified in this population. In subgroup A, 125 subjects were submitted to P, AFBE and flexible pansigmoidoscopy (FP). Percentage of screened tumors is 19.2%. Sensitivity rate of radiology for exploration of the recto-sigmoid area, as compared to FP is rather low: 0.41. In subgroup B, 165 subjects were submitted to hemoccult, P, AFBE and colonoscopy when an abnormal or dubious image was shown by AFBE. The comparative study of these different means of investigation shows a very low rate of sensitivity of hemoccult: 0.16. In addition, the percentage of screened colorectal tumors is significantly higher (p less than 0.01) in subjects with personal or family history of polyp or carcinoma: 22%, compared to the incidence in the remaining population of 13%. Flexible pansigmoidoscopy is recommended for systematic screening of colorectal tumors in subjects older than 40. (Author abstract) (29 Refs)

5. STREPTOCOCCUS BOVIS BACTEREMIA: DIAGNOSIS OF NEOPLASMS BY COLONOSCOPY.

Manzella JP
Div. Infectious Diseases, Dept. Medicine, Yogk Hosp., 1001 S George St., York, PA, 17405
South Med J; 74(8):999-1000 1981

An adenocarcinoma at the ileocecal valve, a pedunculated polyp, and a benign adenomatous polyp, respectively, were discovered by colonoscopy in three patients (a woman age 87 yr and two men age 63 and 71 yr) with Streptococcus bovis bacteremia. Barium enema studies in these patients had shown no abnormality in one case and diverticular disease in two cases. The results of a published study of 29 patients with S bovis bacteremia revealed colonic lesions in 11/15 patients who had a complete gastrointestinal evaluation, including colonoscopy, compared with 4/14 patients who had incomplete gastrointestinal evaluation. It is suggested that colonoscopy would have discovered more neoplastic lesions in the latter group. (5 Refs)

6. EARLY DIAGNOSIS OF RECTAL CANCER.

Bolanca A, Soljan N, Kovacevic I
Dept. Surgery and Medicine, Univ. Hosp., Dr. Mladen Stojanovic, Sch. Medicine, Univ. Zagreb, Zagreb, Yugoslavia
Am J Proctol Gastroenterol Colon Rectal; 32(8):24-26 1981

Cancer of the colon and rectum is on constant increase. Frequency of this localization in comparison with cancer of other localization, is also on the increase. Of 7,010 performed rectoscopies in the period from 1968 to 1974, 546 neoplasms of the rectum were discovered and 386 were malignant. There were not any differences among sexes. Taking into account the age group, the highest incidence was in the seventh decade. The av period from the first signs of the disease until the establishment of correct diagnosis was 7.5 mo. The diagnosis of the tumor was established in 76.0% of cases by a simple method of digitorectal examination, while 71.2% of cases were found up to 10 cm from the anal opening. In 65.0% of cases, tumor was resectable and in 94.0% histological finding was adenocarcinoma. The introduction of systematic rectoscopy and improvement of coloproctological service (from January 1975 to June 1977 further 1,650 rectoscopies) resulted in significant improvement of early detection and percentage of operable cases. In 92 discovered cancer cases, 73.0% were resectable. Seventeen cases of smaller cancers in very early stage were removed with success during rectoscopy examination itself. (Author abstract) (14 Refs)

7. HISTOPATHOLOGICAL STUDIES OF COLO-RECTAL CANCER CONCERNED WITH INTRAMURAL SPREAD: WITH SPECIAL REFERENCE TO PERINEURAL INVASION.

Ohgai T
First Dept. Surgery, Sch. Medicine, Toho Univ., Ota-ku, Tokyo 143, Japan
Nippon Daicho Komonbyo Gakkai Zasshi; 34(2):91-100 1981

Histopathological studies of colorectal cancer concerned with intramural spread and its relationship to the prognosis were performed in 264 surgical cases; the results are as follows. Lymphatic invasion and venous invasion had a close relationship to the lymph node metastasis and the liver metastasis. Vascular invasion and perineural invasion were influenced by intramural spread of cancer. In the patients with vascular invasion of the bowel wall, the corrected 5 yr survival rate was significantly lower than in the patients without vascular invasion (p less than 0.05). These results suggested that vascular invasion and perineural invasion in the bowel wall were important prognostic factors in patients with colorectal cancer. (32 Refs) (In JPN)

8. A STUDY OF OBSTRUCTING CARCINOMA OF THE LARGE BOWEL.

Shimoyama T, Kitasato S, Takagi T, Nogawa T, Fukuda Y, Harada T, Yoshida C, Nakayama H, Hirano T, Hashimoto S, Fujii R, Setoguchi M, Ishikawa Y, Kotake Y, Ishii T, Uchida Y, Miura T, Tsuji Y
First. Dept. Surgery, Nagasaki Univ., Sch. Medicine, Sakamoto-cho, Nagasaki 852, Japan
Nippon Daicho Komonbyo Gakkai Zasshi; 34(1):18-25 1981

A clinical and pathological study of 30 patients with obstructing carcinomas (11.0%), out of 272 patients with colorectal carcinoma treated at the Nagasaki University Hospital from 1965 to 1979, was made. Sixteen of the patients (53.3%) were female and 14 (46.6%) males. The age ranged from 3 to 86 yr, with an av of 61.5. Most of the tumors (73.3%) were located in the left colon, compared with 26.7% in the right colon. The av duration of symptoms was 3.6 mo. Nineteen patients received resection of the primary lesion (resectability 63.3%) and 38.3% received curative resection. All of the right colon cancers were treated by primary resection, but of the 13 left colon cancers, 7 were treated by primary resection followed by primary anastomosis, 4 by colostomy following Hartmann's procedure, and 2 had a staged resection. Of the 19 resected specimens, 89.5% were histologically adenocarcinomas, 9 of which were diagnosed as well-differentiated adenocarcinoma and 8 as moderately differentiated adenocarcinoma. Mucoid carcinoma and squamous cell carcinoma were seen in one case each. The intestinal obstruction was correlated with serosal invasion. Lymph node metastasis was present in 57.9% of the patients and was histologically lymphangial invasion (57.9%) or venous invasion (84.2%). Postoperative anastomosis leakage was found in three of the patients with primary resection of the left colon, but patients with staged resection and Hartmann's procedures showed good results. The survival period of 14 patients after curative surgery was 1 mo to 12 yr, 10 mo, and the 5-yr survival rate was 44.4%. (Author abstract) (28 Refs) (In JPN)

9. COLORECTAL CANCER IN YOUNG ADULTS.

Bedikian AY, Kantarjian H, Nelson RS, Stroehlein JR, Bodey GP
Dept. Developmental Therapeutics, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner St., Houston, TX, 77030
South Med J; 74(8):920-924 1981

The clinical and pathologic characteristics of colorectal cancer in patients younger than 30 yr are compared with those in patients 30 to 39 yr of age. Patients in the two age groups had similar symptoms, predominantly undifferentiated neoplasms, and poor prognoses. However, when the characteristics of these patients were compared with those described for a general patient population with colorectal cancer there was a gradual decrease in the incidence of mucin-producing tumors, poorly differentiated carcinomas, and primary lesions in the right colon, with increasing age at diagnosis. The highest incidences were found in patients less than 30 yr old. The degree of tumor anaplasia and stage of tumor at diagnosis significantly influenced the duration of disease-free interval after curative resection of the primary and the duration of survival. Ninety-six percent of patients younger than 40 yr had carcinomas extending beyond the colonic wall at diagnosis, adversely affecting long-term survival. The 5-yr survival of only 25% to 30% in these patients emphasizes the need for early diagnosis and aggressive treatment. (Author abstract) (30 Refs)

10. GRANULAR CELL TUMORS OF THE GASTROINTESTINAL TRACT AND PERIANAL REGION. A STUDY OF 74 CASES.

Johnston J, Helwig EB
(c/o Helwig) Dept. Gastrointestinal Pathology, Armed Forces Inst. Pathology, Washington, DC, 20306
Dig Dis Sci; 26(9):807-816 1981

Seventy-four patients with 75 examples of granular cell tumors occurring in the gastrointestinal tract and perianal region were studied. Twenty-four were located in the esophagus, 8 in the stomach, 3 in the small bowel, 4 in the appendix, 20 in the large bowel, and 16 in the perianal region. Nine cases had multiple tumors either occurring in the same area of the bowel or in other organs, mostly the skin. Approx 50% of the tumors occurring in the esophagus and perianal region showed varying degrees of acanthosis or pseudoepitheliomatous hyperplasia. In the perianal tumors the pseudoepitheliomatous hyperplasia was much more extensive and could be mistaken for squamous cell carcinoma. The world literature was reviewed and a total of 66 cases of granular cell tumors were reported in the area of study. In neither our 74 nor the other reported cases was there evidence of recurrence or malignant behavior of the tumors, thus confirming their benign biologic behavior. (Author abstract) (68 Refs)

11. COMPARATIVE STUDY OF VILLOUS, VILLOTUBULAR, AND TUBULAR ADENOMAS IN THE COLON AND RECTUM.

Kozuka S, Nogaki M, Nogaki M, Ozeki T, Masumori S, Kitano H, Koshimura K
Dept. Pathology, Nagoya Univ. Sch. Medicine, Nagoya, Japan
Gan No Rinsho; 27(9):1118-1124 1981

Pathohistological examinations were performed in 712 patients with large intestine polyps, and the size of the lesion, the cancer occurrence rate, age and sex of the patients, etc were studied particularly in 410 patients with tubular adenomas, 115 with villotubular adenomas, and 43 with villous adenomas. The incidence of cancer was 9.0% in the tubular adenoma group, 26.1% in the villotubular adenoma group, and 25.6% in the villous adenoma group. The incidence of cancer among those with tumors that were either 2 cm in diameter or less or greater than 2 cm, respectively, was 7.6% and 48.1% in the tubular adenoma group, 22.8% and 50.0% in the villotubular adenoma group, and 7.4% and 47.6% in the villous adenoma group. Compared to tubular or villotubular adenomas of the same histological grade of malignancy, the villous adenomas were larger in av diameter and were observed more often in elderly patients. (24 Refs) (In JPN)

12. EXTRAMURAL VENOUS INVASION AS A PROGNOSTIC FACTOR OF POSTOPERATIVE LIVER METASTASIS IN COLORECTAL CANCER.

Shida H, Kubo T, Sakamoto M, Oya G
Dept. Surgery, Mitsui Memorial Hosp., Kanada, Chiyoda-ku, Tokyo 101, Japan
Nippon Geka Gakkai Zasshi; 82(3):277-283 1981

Venous involvement of cancer cells in 243 resected specimens of colorectal cancer was examined by van Gieson's elastic tissue stain. Venous invasion was recognized in 100 cases (41%), 44 in the submucosal layer only and 56 in the extramural space. This incidence was not affected by the location or histological grade of the tumor, but was directly related to the depth of the cancer penetration and the presence of lymphatic metastasis. Liver metastases were found in 59 cases either during the operation or in the postoperative period. Venous invasion was noted in 69% of this group. Meanwhile, 41 cases out of 100 with venous invasion and 31 cases out of 56 with extramural venous invasion showed postoperative liver metastasis. Curative operations were performed in 175 cases. Ninety-three cases were followed over 3 yr, and 63% of the cases with extramural venous invasion in this group revealed postoperative liver metastasis. There was no significant relationship between lymph node involvement and metachronous liver metastasis. It is suggested that extramural vein invasion may be valuable in the prognostic evaluation of colorectal cancer for development of postoperative liver metastasis. (Author abstract) (30 Refs) (In JPN)

13. COLORECTAL POLYPS IN JUVENILE PATIENTS WITH SPECIAL REFERENCE TO MULTIPLE WELL-DIFFERENTIATED ADENOMAS AT THE ANORECTAL JUNCTION.

Kozuka S, Nogaki M, Nogaki M, Nogaki M, Ozeki T, Masumori S
Dept. Pathology, Nagoya Univ. Sch. Medicine, Nagoya, Japan
Gan No Rinsho; 27(10):1214-1220,A-58 1981

Seventeen patients (11 male, 6 female) who were less than 20 yr old and had large intestinal polyps were reported, and the histological differences between the resected polyps, adenomas, and metaplastic polyps were discussed. Four of the patients had multiple well-differentiated adenomas of the anorectal junction; tubular adenoma was observed in one of these four and in three other patients with single polyps, single metaplastic polyps were observed in two, and juvenile polyps were observed in eight. The juvenile polyps were observed 7/8 patients who were less than 10 yr old. Histological examination of the resected polyps from the four patients with multiple polyps showed polyps consisting of large crypts and large amounts of mucus in the epithelial cells, severe pseudostratification of the epithelial cells in a focus of tubular adenoma, epithelial nuclei situated at the base of epithelial cells and hypertrophic glands in the mucosa on the border of a polyp. A metachronous polyp was discovered in the primary site 2 yr 4 mo after the initial complete resection of multiple polyps in the anorectal junction in one of the patients. (19 Refs) (In JPN)

14. DIFFUSELY INFILTRATING CARCINOMA OF THE COLON (LINITIS PLASTICA TYPE).

Vernon SE, Unger HM, Traitz JJ
Dept. Pathology, St. Francis Hosp., 250 West 63rd St., Miami Beach, FL, 33141
Dis Colon Rectum; 24(5):391-394 1981

Diffusely infiltrating carcinoma of the colon with a vigorous stomal desmoplastic response has been referred to as 'linitis plastica' carcinoma of the colon. Only a relatively small number of such cases have been reported. A disproportionate number of these involve younger age groups, and survival as a rule has been poor. We use the term linitis plastica to describe specific patterns of infiltration and desmoplasia that are distinctive from those seen in typical colonic adenocarcinomas. (Author abstract) (13 Refs)

15. LOCALIZATION AND CONCENTRATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN GASTROINTESTINAL TUMORS: CORRELATION WITH CEA LEVELS IN PLASMA.

Wagener C, Muller-Wallraf R, Nisson S, Groner J, Breuer H
(c/o Breuer) Institut fur Klinische Biochemie, Sigmund-Freud Strasse 25, 5300 Bonn 1, W. Germany
JNCI; 67(3):539-547 1981

In 50 patients with gastrointestinal carcinomas, the following tumor parameters were studied: the concentration and localization of carcinoembryonic antigen (CEA) in tissue, extension, invasion, infiltration, differentiation, and necrosis. CEA concentrations were measured in plasma samples of all patients. In seven patients with gastric carcinomas, CEA concentrations in tissue were low. Generally, only single cells or cell groups were CEA-positive. Elevated CEA levels in plasma resulted mainly from distant metastases and not from the primary tumor. In 43 colorectal carcinomas, CEA concentrations in tissue varied between 1.5 and 472 ug/g tissue. They were closely related to the degree of accumulation of CEA-positive necrotic material in the neoplastic glands. In 35 patients with colorectal carcinomas without CEA producing distant metastases, preoperative CEA levels in plasma were normal when tumor necrosis and perineural invasion were absent and CEA concentrations in tissue were low. CEA levels in plasma were regularly elevated when the tumor showed considerable necrosis in the presence of high CEA concentrations in tissue. (Author abstract) (22 Refs)

16. CORRELATIONS BETWEEN SERIAL CEA LEVELS AND SURGERY IN PATIENTS WITH COLORECTAL CARCINOMA.

Midiri G, Amanti C, Benedetti M, Caliento D, Consorti F, Del Buono S, Di Paola M
(c/o Amanti), Clinica Chirurgica IV, Policlinico Umberto I, 00185 Roma, Italy
J Surg Oncol; 17(4):341-344 1981

Nowadays the evaluation of serial carcinoembryonic antigen (CEA) levels represents an important parameter for the prognosis of patients with carcinoma of the large bowel. Changes in CEA values allow the drawing of conclusions regarding the effectiveness of therapy. We have studied 63 patients with colorectal carcinoma that underwent surgical treatment. Serial CEA levels were tested in each patient before surgery and 15 days after. The 53 patients were considered surgically cured; and among these 7 did not have a significant decrease of CEA values after surgery. The percentage of recurrences among these patients has been 71.4%; meanwhile patients who showed a decrease of CEA values below cutoff values had recurrences only in 17.3% of cases. For this reason it is our opinion that patients considered surgically cured who have postoperative high CEA levels cannot be considered really cured from a biological point of view. (Author abstract) (19 Refs)

17. CLINICAL STUDIES OF CARCINOEMBRYONIC ANTIGEN (CEA) IN TUMOR TISSUE AS A PARAMETER FOR DETERMINING THE PROGNOSIS OF COLON CANCER; COMPARISON OF HISTOLOGICAL STAGE AND CEA VALUE IN THE BLOOD (MEETING ABSTRACT).

Hamada Y, Yamamura M, Koyama H, Takada H, Hioki K, Yamamoto M
Dept. Surgery, Kansai Medical Univ., Moriguchi-shi, Osaka Pref. 570, Japan
Nippon Geka Gakkai Zasshi; 82(Suppl):172 1981

CEA staining by the enzyme antibody method was performed on 16 colon cancers and 40 rectal cancers. Eleven well differentiated adenocarcinomas and 36 moderately differentiated adenocarcinomas were classified according to their CEA staining ability: localized staining type (Grade I), tubular secretion type (Grade II) and interstitial infiltration type (Grade III). Histologically, all 49 adenocarcinomas, 2 mucinous carcinomas and 2 signet ring cell carcinomas were positive for CEA, and 3 squamous cell carcinomas and 1 malignant lymphoma were negative, giving a positive CEA staining rate of 92.8%. According to Duke's classification, the positive rate of CEA in the blood was 30%, 58% and 84% for A, B and C types, respectively, which reflected the stage of cancer. The CEA positive rate in the blood was 16.7%, 70.3% and 100% for grades I, II and III, respectively. The grade was advanced in moderately differentiated adenocarcinoma and in adenocarcinoma invading into the proper muscle and beyond. Lymph node metastasis was found in 0%, 48% and 100% of grades I, II and III, respectively. However, lymphatic invasion and max tumor diameter were not related to the grade. This graded classification of CEA in tumor tissue was considered to be a good parameter for foreseeing and determining the clinical stage of colon cancer. (no Refs) (In JPN)

18. CARCINOEMBRYONIC ANTIGEN LEVELS AS AN INDICATOR OF THE PRIMARY SITE IN METASTATIC DISEASE OF UNKNOWN ORIGIN.

Koch M, McPherson TA
Dept. Medicine, Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta, T6G 1Z2, Canada
Cancer; 48(5):1242-1244 1981

In 542 patients with metastatic disease arising from a known primary site, elevated CEA levels (greater than 10 ng/ml) were most often associated with metastatic disease originating from entodermally derived organs, breast, and mucinous ovarian primaries. This observation held true, in general, in a small series of 32 patients with metastatic disease arising from a primary site that had been unknown, but that was eventually identified. Thus, although a CEA level below 10 ng/ml is of no use in pointing to a particular primary site, a value above 10 ng/ml suggests the site is more likely to be in an entodermally derived organ, breast or ovary containing a mucinous carcinoma. If liver metastases are present, there is an increased probability that the primary site will be found in the large bowel or pancreas. (Author abstract) (9 Refs)

19. CEA: BASIC CONCEPTS, CLINICAL APPLICATIONS.

Reynoso G
Dept. Pathology, Ideal/Wilson Medical Center, Johnson City, NY
Diagn Med; 4(4):41,42,46-48,51,54-57 1981

Review of diagnostic potential engendered in the association between oncogenesis and integrity of the immunocompetent system is supported by an assessment of carcinoembryonic antigen (CEA) and its clinical application. CEA is a glycoprotein that is abundant in entodermally-derived tissues (intestinal mucosa, pancreas, lung) and also found in non-entodermally derived tissues. Present in normal fetal tissues, it is also an oncofetal antigen, ie a tumor-associated antigen that reappears in adult cells and plasma during oncogenesis. CEA is the only immunological test for cancer with widespread clinical use. Biochemical characterization and tentative structure have been made. Many glycoproteins exhibit immunological cross-reactivity with CEA extracted from colonic carcinoma tissue; these glycoproteins are thought to belong to a single class of closely related antigens sharing four classes of antigenic determinants. Use of CEA in cancer screening programs for asymptomatic populations is not efficient: CEA appears in normal cells and incidence of antigenemia in healthy subjects increases with age and level of smoking. Neither the sensitivity nor specificity of CEA assays is high enough to justify its use alone as a diagnostic test; additional studies are needed in patients with consistently elevated levels of CEA. CEA can be used as an adjunct in cancer patient management, to aid in clinical staging and detect recurrence or relapse in surgically treated cases, and to monitor treatment in patients undergoing chemo- or radiotherapy. CEA is most reliable for monitoring colorectal cancer and possibly mammary and pancreatic carcinoma and neuroblastoma. (50 Refs)

20. STUDIES OF LYMPHOCYTE PROLIFERATIVE RESPONSE TO AUTOLOGOUS TUMOR EXTRACT IN VARIOUS CANCER PATIENTS.

Honjo H
First Dept. Surgery, Nihon Univ., Sch. Medicine, Itabashi-ku, Tokyo 173, Japan
Nichidai Igaku Zasshi; 40(2):129-139 1981

Lymphocyte proliferative responses to the autologous tumor extract (LP responses) were examined in 53 patients with various cancers. Preoperatively, positive LP responses stimulation index (SI) of 2.00 or greater were observed in 19 patients. Analysis of the positive responders according to the histological type of the tumor revealed that patients with neuroblastoma gave the most frequent positive responses, followed in order by colorectal, stomach and breast cancer patients. Analysis of the relationship between the frequency of positive responses and extent of disease revealed that patients with intermediate disease gave the most frequent positive responses, followed in order by those with widespread and localized disease. No statistically significant relationship was observed between the LP responses and prognosis of the disease or lymphocyte proliferative responses to phytohemagglutinin. Serial determinations of the LP responses in adult cancer patients revealed that the SI values of patients who had curative surgery fell to low levels at about 6 mo after the operation and remained low until recurrence developed. On the other hand, in patients who had noncurative surgery, SI values were highest preoperatively, decreased after surgery and remained low. Serial determinations of the LP responses in children with cancer revealed that the SI values fell to low levels after complete or partial tumor removal and remained low until recurrence or tumor regrowth was detected clinically. (25 Refs) (In JPN)

21. IN VIVO AUGMENTATION OF NATURAL KILLER (NK) ACTIVITY BY A STREPTOCOCCAL PREPARATION, OK-432: CHARACTERIZATION OF EFFECTOR CELLS AND INDUCTION OF INTERFERON IN SERA.

Wakasugi H, Miyata M, Morioka Y, Oshimi K, Kasahara T, Takahashi K, Saito M, Ebina T

Dept. Surgery, Jichi Medical Sch., Japan

Nippon Gan Chiryo Gakkai Shi; 16(3):433-446 1981

The effects of pre- and/or postoperative treatment with streptococcal preparation OK-432 on natural killer (NK) cell activity and interferon titers were studied in 40 patients with stomach, breast, pancreas, or colon cancer. The patients received a first OK-432 course beginning on postoperative days 7-35 (Group I) or a second course beginning on postoperative days 8-52 (Group II), 6-20 (Group III), or 5-43 (Group IV). Patients in Groups I, II, and III showed significantly augmented killer cell activity within 3 days of initial OK-432 inoculation. Characterization of effector cells from Group IV patients showed that they were NK cells (T and non-T cells and IgG-Fc receptor-positive cells). Induced IF titers studied in Groups I, II, and III did not correlate with levels of augmented NK activity. Four Group III subgroups were distinguished according to degree of NK activity and IF titers: patients with low IF titers that declined with augmented NK activity, patients with low titers that increased with augmented NK activity, patients in whom IF was detected continuously without NK augmentation, and patients with augmented NK activity but no significant IF induction. (40 Refs) (In JPN)

22. CELL-MEDIATED IMMUNITY INDICES IN PATIENTS WITH RECTAL TUMORS AFTER SURGERY AND COMBINED THERAPY.

Evsev'eva AI, Mosienko MD, Zybina MA, Umansky YuA

R. E. Kavetsky Inst. Oncology of Acad. Sciences of Ukrainian SSR., Kiev, USSR

Vopr Onkol; 27(6):40-44 1981

The dynamics of cell-mediated immunity indices in 83 patients with rectal tumors who underwent surgery or received combined treatment (preoperative radiation and surgery) was followed. Cellular immunity was assessed on the basis of PHA-induced blastogenic reaction of lymphocytes (BRL) and spontaneous rosette-formation. In rectal tumor patients, particularly at Stage IV, the level of PHA-induced BRL and the total number of rosette-forming cells (RFC) were lower than in healthy donors. Surgery did not produce any significant changes in cell-mediated immunity parameters: level of PHA-induced BRL decreased by 16,7%, while total RFC number increased by 17.2% (mostly low-affinity forms). Preoperative radiation resulted in a significant decrease in lymphocyte ability to undergo PHA-induced blast-transformation (45%) and spontaneous rosette formation, high-affinity lymphocytes being most sensitive to ionizing radiation. Their fraction decreased by half. (Author abstract) (18 Refs) (In RUS)

23. BILE ACIDS IN THE FECES AND THEIR RELATION TO COLON CANCER: COMPARATIVE STUDIES OF JAPANESE AND AMERICANS (MEETING ABSTRACT).

Takahashi M, Kodama M, Tamura T, Ezaki H, Hoshita T, Cohen BI
Dept. Surgery, Chugoku Rosai Hosp., Kure-shi, Hiroshima Pref. 737-01, Japan
Nippon Geka Gakkai Zasshi; 82(Suppl):168 1981

Feces of Japanese and Americans were examined for sterols and iso-bile acids having a hydroxy group at the 3beta position, since the risk of developing colon cancer is greater in Americans than in Japanese. The concentration of bile acid in the feces was 7.5 +-3.4 mg/g of feces for healthy Americans (n=16)and 10.3 +-5.3 mg/g of feces for Americans with colon cancer (n=12). On the other hand, the concentration in the feces of healthy Japanese and those with colon cancer was 2.9 +-1.4 (n=10) and 3.8 +-0.7 mg (n=10), respectively. While the bile of the Americans consisted of only secondary bile acids, that of the healthy Japanese and Japanese with colon cancer was comprised of 33% and 10% primary bile acids, respectively. The percentage of iso-bile acids (isolithocholic acid + isodeoxycholic acid), which are considered to be produced by the intestinal flora, was 33% and 32%, respectively, for the healthy Americans and Americans with colon cancer, while it was 16% and 31%, respectively, for the healthy Japanese and Japanese with colon cancer. When methylnitrosourea (MNU) was injected into the intestines of rats, the percentage of rats which developed colon tumors was 49%, but when MNU was given together with isolithocholic or lithocholic acid, it was 46% and 65%, respectively, only lithocholic acid having a colon cancer-promoting effect. (no Refs) (In JPN)

24. FALSE-NEGATIVE RESULTS OF HEMOCCULT TEST IN COLORECTAL CANCER.

Griffith CD, Turner DJ, Saunders JH
Gastrointestinal Unit, Western General Hosp., Edinburgh EH4 2XU, Scotland
Br Med J; 283(6289):472 1981

The testing for fecal blood using the Hemoccult test is described through the prospective study of 28 patients with histologically proved carcinomas of the colon and rectum. The stools were positive in 23 patients, 21 of whom had ulcerated tumors. The results thus indicated that ulceration of the tumor is an important factor in the false-negative hemoccult reaction. It was suggested that nonulcerated tumors are less likely to bleed into the lumen of the bowel, and hence a negative test result for fecal occult blood would result despite the presence of a carcinoma. (5 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

25. SURGICAL TREATMENT OF CANCER OF THE COLON.

Stefanini P, Castrini G, Pappalardo G
(c/o Castrini) 2nd Surgical Clinic, Univ. Rome Medical Sch., Policlinico Umberto I, 00161 Rome, Italy
Int Surg; 66(2):125-131 1981

The authors give a brief review of the course of surgical treatment for colon cancer in the last two decades, as reported in the medical literature. Between 1960 and 1980 they examined 619 patients. Of these 599 underwent surgery: 436 (72.8%)

had radical surgery and 163 (27.2%) received palliative operations. The morbidity was 12.1% and the mortality 2.7%. Sixty percent of patients in Dukes' class 'A' and 'B' were alive after 5 yr, against 28% of those in class 'C' and none in class 'D'. The results obtained during the 1970 to 1980 period are not significantly better than those obtained from 1960 to 1969. On the basis of this experience, the authors describe their present approach for the treatment of tumors of the colon and explain in detail the preoperative preparation of the patients, the extension of the excisions and of the lymphectomies, according to the site of the cancer and its local or distant invasion, the use of temporary derivative colostomies and the application of additional medical therapies. Guidelines for reaching an early diagnosis of colon carcinoma are given, in order to improve the postoperative survival rate. (Author abstract) (26 Refs)

26. 'RISK FACTORS' IN SURGICAL TREATMENT OF CANCER OF THE COLON.

Eriukhin IA, Silin BN, Akinchev SL
Leningrad, USSR
Vestn Khir; 126(6):46-51 1981

Of 229 patients with cancer of the colon seen between 1965 and 1979, 181 underwent surgery. Radical surgery was performed in 149/181 patients. The incidence of postoperative complications depended upon the stage of disease (complications were recorded in 1/7 patients with Stage I, 9/26 with Stage II, 60/97 with Stage III, and 41/51 with Stage IV) and the age of the patients (complications were recorded in 83/118 patients greater than 50 yr old and in 28/63 patients less than 50 yr old) Majority of the postoperative complications were recorded in the patients with complicated course of the disease (infiltration, perforation, abscess, lymphangitis, intestinal obstruction). (14 Refs) (In RUS)

27. PATTERNS OF RECURRENCE FOLLOWING CURATIVE RESECTION ALONE FOR ADENOCARCINOMA OF THE RECTUM AND SIGMOID COLON.

Rao AR, Kagan AR, Chan PM, Gilbert HA, Nussbaum H, Hintz BL
Dept. Radiotherapy, Southern California Permanente Medical Group, 1510 North Edgemont, Los Angeles1, CA, 90027
Cancer; 48(6):1492-1495 1981

Two-hundred-four patients with previously untreated adenocarcinoma of rectum, rectosigmoid, and sigmoid colon were retrospectively evaluated to determine patterns of recurrence following curative resection. Seventy-eight (38%) subsequently developed recurrent disease. Of these, 40% (31/78) presented with local recurrence alone, 28% (22/78) with regional recurrence, 15% (12/78) with concomitant local recurrence and distant metastasis, and 17% (13/78) with distant metastasis alone. The degree of tumor anaplasia and depth of tumor penetration into the bowel wall influenced the rate of local recurrence. Through 5 yr, local recurrence without clinical evidence of distant metastasis was the most common cause of death. Need for adjuvant radiation therapy is discussed. (Author abstract) (18 Refs)

28. THE RELATIONSHIP BETWEEN THE SHORTEST DISTANCE FROM THE TIP OF THE CANCER TO THE EXTERNAL SURGICAL SURFACE IN CANCER OF THE LOWER RECTUM (MEETING ABSTRACT).

Ohmi Y, Eguchi H, Oki S, Tsujinaka Y, Nakamura K, Tajima S, Umemoto M, Matsushima M, Iida A, Yamaoka H, Jo T, Inuo T, Tsuchiya S
Second Dept. Surgery, Yokohama City Univ., Sch. Medicine, Minami-ku, Yokohama 232, Japan
Nippon Geka Gakkai Zasshi; 82(Suppl):170 1981

Radical rectal excision accompanied by upper and lateral lymph node dissection was performed on 60 patients with cancer of the lower rectum. The distance from the tip of the cancer to the external surgical surface (ew) was measured from various sites of the main lesion, and the shortest distance was determined. The site from which ew was obtained was macroscopically at the center of the cancer lesion in 24 patients, and it was at the deepest site of intramural invasion in 36 patients. The ew was significantly shorter (p less than 0.05) in the 12 patients who had local recurrence than in the 25 patients who did not, and local recurrence occurred in 80% of the five patients with ew of less than 1 mm. Local recurrence did not occur in the 12 patients with cancer that invaded into or beyond the proper muscle, but occurred in 9 of 21 of the patients with cancer not invading into the other organs but beyond the proper muscle (a2) and in 3 of the 4 patients with cancer invading into the other organs (ai). The shortest ew of the patients without local recurrence was 4 mm, 3 mm and 2 mm, respectively for cancer of the anterior, posterior and lateral walls with a2 invasion, while it was 6 mm for ai. Combined resection of the regions near the prostate or posterior wall of the uterus was not sufficient to prevent local recurrence in a2 cancer. There were no recurrences when ew was 6 mm or more. The max thickness of the soft tissue surrounding the rectum that could be resected was less than 1 mm of the anterior wall, about 6 mm of the posterior wall and 8-10 mm of the lateral wall. (no Refs) (In JPN)

29. COLONIC MUCOSAL-SUBMUCOSAL BLOOD FLOW AND THE INCIDENCE OF FAECAL FISTULA FORMATION FOLLOWING COLOSTOMY CLOSURE.

Forrester DW, Spence VA, Walker WF
St. James's Univ. Hosp., Leeds LS9 7TF, England
Br J Surg; 68(8):541-544 1981

Fistula formation following closure of a colostomy occurs most frequently when closure is carried out within the 1st few wk of construction and may be related to an impaired local microcirculation. Using a recently described method for measuring colonic mucosal-submucosal blood flow, the variations in local flow which occur during the 1st mo after colostomy construction were determined in eight patients. Mean blood flow increased from 6.9 +-1.8 ml min-1 100 g-1 (sd) at 7 days to 31.1 +-12.5 ml min-1 100 g-1 (sd) at 28 days. In a further 40 consecutive patients undergoing colostomy closure, blood flow measurements were made before operation. Eight patients developed a fecal fistula, and in five of these patients mucosal-submucosal blood flow was found to be less than 15 ml min-1 100 g-1. In every successful colostomy closure blood flow was greater than 15 ml min-1 100 g-1. This study provides evidence that a subnormal blood flow is one of the factors associated with fistula formation following the operation of colostomy closure. (Author abstract) (16 Refs)

30. PELVIPERINEAL RECURRENCES IN CARCINOMA OF THE RECTUM.

Garavoglia M, Bargoni A, Discalzo L, Fronticelli CM, Conti F
Instituto di Anatomia Chirurgica, Universita di Torino, Torino, Italy
Minerva Chir; 36(11):771-776 1981

In the period 1970-1980, radical perineal-abdominal surgery was performed in 108 cases of rectal carcinoma: 70 were anterior resection and 38 abdominoperineal amputation. Relapse occurred in 23 cases (13 males and 10 females, 49-77 yr old). Of these 17 had had anterior resection and 6 abdominoperineal amputation. For anterior resection relapse, latency period was 3-72 mo and survival time 8 mo to greater than 4 yr after surgery. In abdominal amputation cases, the relapse latency period was 4-12 mo and survival time was 8-36 mo. Biological behavior of the tumor, involvement of the rectal wall, and lymphatic diffusion were major causes of relapse. The selection of anterior resection in some cases of middle rectum carcinoma can be a determining risk factor. (21 Refs) (In ITA)

31. MORPHOLOGICAL EVALUATION OF THE EFFICACY OF PREOPERATIVE GAMMA THERAPY OF RECTAL CANCER.

Vasil'eva NN, Lukina TA>, Barsukov IuA, Knysh VI, Aliev BM
Cancer Res. Center, Moscow, USSR
Med Radiol (Mosk); 26(7):32-39 1981

Comparative efficacy of different variants of preoperative gamma therapy was evaluated in 43 patients with adenocarcinoma of the rectum. Group I (21 patients) received irradiations from open fields (single dose 400 rads, total dose 2,000 rads) and Group II (22) received irradiations through the grid diaphragm (single dose 1,000 rads, total dose 5,000 rads in 5 consecutive days). Biopsy specimens obtained prior to radiotherapy and surgery specimens were examined histocytologically. Radiation injury of the II and III degree (necrosis and dystrophy of one third and two thirds of the tumor, respectively, enhanced production of the mucus) was recorded in 66.7% of the patients in Group I and in 60% of the patients in Group II. Irradiation through the grid diaphragm provided more effective protection of the adjacent normal tissues. (16 Refs) (In RUS)

32. INTERSTITIAL HYPERTHERMIA AND INTERSTITIAL IRIDIUM 192 IMPLANTATION: A TECHNIQUE AND PRELIMINARY RESULTS.

Joseph CD, Astrahan M, Lipsett J, Archambeau J, Forell B, George FW
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Int J Radiat Oncol Biol Phys; 7(6):827-833 1981

The feasibility of combining interstitial hyperthermia (41-43 C, for 30-40 min) with interstitial Iridium 192 implantation (Ir-192, 2,000-3,000 rad) in the treatment of superficially accessible tumors has been tested on swine and confirmed in seven patients (3 with primary breast cancer, 1 with neck nodes from a tongue primary, and 3 with sc metastases from malignant melanoma or colon primaries). Therapy protocol consisted of external beam radiotherapy (3,000-4,000 rad in 3-4 wk), followed successively by 3 wk rest, the first hyperthermia session, Ir-192 implantation, and a second hyperthermia session. Techniques and instruments used for positioning the thermal probes and implants are described. (4 Refs)

33. THE EFFECTS OF CONCOMITANT USE OF NEOCARZINOSTATIN (NCS) AND 5-FLUOROURACIL (5-FU) AS ADJUVANT CHEMOTHERAPY OF CANCER OF THE LARGE INTESTINE.

Yokomori T, Taniguchi T, Hisataka H, Kaneko H, Owada S, Saito K, Watanabe M
Dept. Surgery, Ojiya General Hosp., Ojiya-shi, Niigata Pref. 947, Japan
Gan To Kagaku Ryoho; 8(4):633-639 1981

Sixty postoperative patients with cancer of the large intestine (27 cases of colon cancer, 33 cases of rectum cancer) were given neocarzinostatin (NCS) in combination with 5-fluorouracil (5-FU) as adjuvant chemotherapy (NF-therapy) and studied for efficacy, side effects and changes of the serum carcinoembryonic antigen value during the therapy. Side effects occurred in 18 cases (30%). There was no difference in incidence of side effects among the various stages of cancer and the operative procedures. Side effects appeared to be more frequent between day 11 and 20 of initiation of treatment. General side effects were leukopenia (11.7%), thrombopenia (5.0%) anorexia (6.7%) and diarrhea (6.7%). In 25 patients treated with nonradical surgery, 14 survived more than 12 mo and 2 more than 24 mo. Out of 23 evaluable cases on the basis of the assessment criteria of Karnofsky, 6 cases (26.1%) were placed in a group of O-A, O-B and O-C, and 8 cases (34.8%) were placed in a group of I-A and I-B. As for the correlation between the period of treatment and the survival duration, both Karnofsky effective cases and long surviving cases treated with surgical resection were mainly observed in the long NF-therapy group. Both the cured patients treated with surgical resection and the patients who showed a high value of serum CEA before surgical resection were placed in Stage I-IV and these showed normal values of serum CEA during the NF-therapy. On the other hand, the noncured patients treated with surgical resection were placed in Stage IV-V and showed variability in serum CEA particularly; the cases with liver metastasis did not show a tendency to decrease in CEA value after NF-therapy. (15 Refs) (In JPN)

34. FLUOROURACIL, IMIDAZOLE CARBOXAMIDE DIMETHYL TRIAZENO, VINCRISTINE, AND BIS-CHLOROETHYL NITROSOUREA (FIVB) IN COLON CANCER.

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Cancer Chemother Pharmacol; 6(1):31-34 1981

The results of treatment of 160 metastatic colon cancer patients with a regimen that included FIVB (fluorouracil, imidazole carboxamide dimethyl triazeno, vincristine, and bis-chloroethyl nitrosourea) were examined in relation to patient discriminants, drug scheduling and administration, and ancillary treatment. The major side effects encountered were hematopoietic suppression, nausea and vomiting, diarrhea, and alopecia. Complete (CR) or partial (PR) remission was observed in 38% of the patients with metastatic colon cancer treated with FIVB who had had no prior chemotherapy exposure. CR or PR was achieved in 26/59 previously untreated patients with a performance status (PS) of 0-1, and in 17/53 patients with a PS of 2-3. A response was achieved by 31/66 patients in whom a wt loss of less than 10 kg had been recorded at the start of treatment, and by 12/46 amongst whom a wt loss of greater than or = was recorded at the start of treatment. Among patients with prior exposure to chemotherapy, the response rate was 20%. Of the patients with no prior chemotherapy, 56%

were considered to have benefited from the treatment. The median duration of remission for the 43 patients without prior chemotherapy who responsed to FIVB was 5.2 mo. The median survival for all 112 patients was 8.4 mo. Median survival for responders was 10 mo, and that for nonresponder, 5.4 mo. (15 Refs)

35. PHASE I-II TRIAL OF METHYL-GAG IN ADVANCED COLON CANCER. A SOUTHWEST ONCOLOGY GROUP PILOT STUDY.

Myers JW, Knight WA, Livingston RB, Fabian C, Costanzi J
Operations Office, Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, KS, 66103
Cancer Clin Trials; 4(3):277-279 1981

Forty-four patients with advanced colon or rectal cancer were treated with methyl-GAG on a weekly schedule. Of the 40 evaluable patients, 35 (87%) had received prior chemotherapy. Objective tumor regression was seen in six patients (1 CR, 5 PR's). An additional nine patients had stable disease for a median of 42 wk. The median survival (42+ wk) for responding and stable disease patients was significantly better ($p = 0.0001$ Wilcoxan test) than those with progressive disease (11 wk). Toxicity was reversible and included mild to moderate mucositis, nausea, vomiting, diarrhea, and thrombocytopenia. Responses observed in this study warrant further trials in patients with colon cancer who have received no prior chemotherapy. (Author abstract) (6 Refs)

36. PHASE II EVALUATION OF METOPRINE WITH LEUCOVORIN RESCUE IN PATIENTS WITH ADVANCED COLORECTAL CARCINOMA.

Lynch G, Currie V, Kemeny N
(c/o Kemeny) Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Clin Trials; 4(3):281-283 1981

In a Phase II trial 24 patients with measurable metastatic colorectal carcinoma were treated every 2 wk with high-dose metoprine at 175 mg/m2 and leucovorin rescue. Hematologic toxicity was mild; the limiting toxicity was CNS, occurring in 54% of the patients. No responses were observed, but four patients had disease stabilization. High-dose metoprine with leucovorin rescue appears ineffective in previously treated patients with colorectal carcinoma in the dose and schedule used in this study. (Author abstract) (7 Refs)

37. CLINICAL OBSERVATION OF 5-FLUOROURACIL (5-FU) CARDIOTOXICITY.

Okuma K, Ota K
Second Dept. Internal Medicine, Aichi Cancer Center Hosp., Chikusa-ku, Nagoya 464, Japan
Gan To Kagaku Ryoho; 8(2):256-261 1981

Clinical records of 385 cancer patients (228 males, 29-93 yr in age; 157 females, 22-84 yr in age) were estimated to investigate 5-fluorouracil (5-FU) cardiotoxicity. There were 181 patients with primary gastric cancer, 62 with primary cancer of the large intestine, 16 with primary cancer of other digestive organs, 52 with primary breast cancer, 38 with primary lung cancer, 10 with primary cancer of the bladder, 15 with primary cancer of the head and neck, and 13 with other primary cancer. In 379 patients with non-cardiac disease, the overall incidence of electrocardiogram (ECG) changes was 1.8% (7 patients), but no patient developed stenocardia or heart failure. On the other hand, ECG changes obtained from the cardiac disease group were not attributable to 5-FU treatment. Since these patients showed anemia or hypopotassemia, these factors may also induce the ECG changes. In this study no patient developed reproducible stenocardia with ischemic ECG changes. This study does not provide any conclusive data in relation to 5-FU cardiotoxicity. Prospective ECG monitoring studies are necessary. (Author abstract) (11 Refs) (In JPN)

38. APPLICATION OF TOTAL PARENTERAL NUTRITION (TPN) AGAINST ADVANCED CLINICAL EFFECTS OF CONTINUOUS INTRAVENOUS ADMINISTRATION OF FUTRAFUL IN COMBINATION THERAPY.

Takahashi M, Asai T, Miura Y, Machida T, Kano K, Ikeuchi H, Yoshida K

Dept. Surgery, Miyagi Prefectural Center for Adult Diseases, Natori-shi, Miyagi Pref. 981-12, Japan

Gan To Kagaku Ryoho; 8(2):314-322 1981

Out of 311 TPN cases since 1974, 99 cases of advanced cancer (8 carcinomas of the esophagus, 57 stomach cancers, 7 carcinomas of the large intestine, 11 cancers of the liver and/or bile duct and/or pancreas, and 16 other malignant tumors) were evaluated. Effect of TPN against advanced cancer differed significantly with regard to the prognosis of the patients, depending upon the condition of the disease, and there was a limited effect in cases of hemorrhage and jaundice. On the other hand, the 5-fluorouracil (5-FU) level was high in the blood and tumor tissue after combination of continuous iv infusion of 1,200 mg/body/day of Futraful and the 5-FU level in the tissue:in the blood ratio was about 3.0. Side effects were relatively mild and a clinical response was observed in 11 out of 26 cases (42.3%) of advanced cancer. (Author abstract) (25 Refs) (In JPN)

39. PHA-STIMULATED LYMPHOCYTE INJECTION THERAPY FOR ADVANCED DIGESTIVE CANCER.

Shimizu N, Izumi A, Kanayama H, Osaki Y, Maeta M, Koga S

First Dept. Surgery, Tottori Univ. Sch. Medicine, Tottori, Japan

Nippon Gan Chiryo Gakkai Shi; 16(2):177-182 1981

Eight patients (7 men, 1 woman; 38-70 yr old) with advanced digestive organ cancer (4 gastric cancer, 1 residual gastric cancer, 1 esophageal cancer, 1 transverse colon cancer, and 1 recurrent small intestine cancer) were administered phytohemagglutinin(PHA)-stimulated lymphocytes in combination with mitomycin C, futraful, and 5-fluorouracil or picibanil. Evaluation of the effects of the therapy was based on Karnofsky's evaluation standards, the Japanese Ministry of Health's criteria for evaluating therapy for solid tumors, and Zubrod's performance standard. Lymphocytes were obtained from normal adults, cultured with PHA, and then injected 2x/wk (total 5 x) into the patients. Of the eight patients, only one showed any clinical effect from the injection therapy. Seven of the eight patients died from 1-5 mo after the therapy was initiated, and one patient was alive 10 mo after therapy began. Five of the eight patients had side effects such as fever, chills, nausea, and dyspnea. The evaluation showed that injection of PHA-stimulated lymphocytes was no more clinically effective than the previous method of injecting allogeneic WBC. (19 Refs) (In JPN)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLO-RECTAL NEOPLASMS

40. COLON POLYPS: WHEN ARE THEY MALIGNANT?

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Geriatrics; 36(8):57-60 1981

A clinical review is made of diagnostic approach, etiology, size and shape, and treatment for polyps of the colon and rectum. The different histologic entities include non-neoplastic (inflammatory, infectious, and hyperplastic), neoplastic (adenoma, carcinoma and sarcoma, metastatic, and others), and miscellaneous (polyposis cystica profunda, pneumatosis cystoides, intestinalis, Cronkhite-Canada syndrome, hamartoma, and juvenile polyp). Diagnosis should involve history and physical examination, and, as indicated, stool studies, flexible fiberoptic sigmoidoscopy, air-contrast barium enema, and colonoscopy. Etiology of polyps is not known, but the various syndromes can be summarized. Those involving high risk of malignancy are familial polyposis, Gardner's syndrome, disseminated gastrointestinal polyposis, and Turcot's syndrome. Low risk diseases are Peutz-Jeghers syndrome, juvenile polyposis and variants, and multiple adenomas. Cronkhite-Canada syndrome and Cowden's disease present no known risk. Polyps less than 5 mm are not usually cancerous, but should be removed or watched closely after biopsy. Those greater than 2 cm are much more dangerous: the incidence of malignancy is in the range of 10-50%. The majority of polyps can be removed by snare cautery at the same time of colonoscopy, even in very sick patients. The two most common complications are perforation (0.22%) and hemorrhage (1.9% with polypectomy). (11 Refs)

41. MULTIPLE JUVENILE POLYPOSIS. A STUDY OF THE PATHOGENESIS OF JUVENILE POLYPS AND THEIR RELATIONSHIP TO COLONIC ADENOMAS.

Lipper S, Kahn LB, Sandler RS, Varma V
Dept. Pathology, Long Island Jewish-Hillside Medical Center, New Hyde Park, NY, 11042
Hum Pathol; 12(9):804-813 1981

Solitary juvenile polyps are common lesions whose pathogenesis is poorly understood. Multiple juvenile polyposis is characterized by large numbers of these lesions either confined to the colon or throughout the gastrointestinal tract. A study of two cases of multiple juvenile polyposis provided fresh insight into the pathogenesis of juvenile polyps and their relationship to colonic adenomas. Mucosal ulceration in very early lesions, together with glandular epithelial calcification, suggested that impaired cell renewal resulting from disturbed regenerative kinetics may predispose to surface epithelial erosion, setting in motion a cycle of ulceration, inflammation, and granulation tissue formation. We postulate that a dyskinetic continuum may link juvenile, 'metaplastic,' and adenomatous polyps. The finding in our second case of multiple adenomatous lesions, including a villoglandular polyp, emphasizes the neoplastic potential of juvenile polyposis. (Author abstract) (37 Refs)

42. SYMPTOM DURATION AND SURVIVAL PROSPECTS IN CARCINOMA OF THE RECTUM.

McDermott F, Hughes E, Pihl E, Milne BJ, Price A
Dept. Surgery, Monash Univ. at Alfred Hosp., Victoria, Australia
Surg Gynecol Obstet; 153(3):321-326 1981

Between 1950 and 1978, 1,228 patients were operated upon by one of us for carcinoma of the rectum. Symptom duration data were available for 1,081 patients. Forty-five percent of the patients had symptoms preoperatively for less than 3 mo, 22% for 3 to 6 mo, 15% for 6 to 12 mo and 18% for 12 mo or longer. The frequency of major symptoms did not differ significantly with increasing symptom duration. Symptom duration was not related to sex, age, tumor site within the rectum or tumor stage distribution. The proportion of curative to palliative operative procedures performed was unrelated to the duration of symptoms. The cancer specific survival rate was better for the total patient series and for those treated by curative resection if symptoms had been present for 12 mo or longer compared with those of less than 3 mo duration, $p = 0.001$ and $p = 0.01$, respectively. Survival prospects were also better for patients with symptoms of less than 6 mo duration compared with those of 6 mo or longer, $p = 0.01$ and $p = 0.04$, respectively. These results indicate that earlier diagnosis during the symptomatic period of carcinoma of the rectum cannot be expected to improve cancer specific survival rates. They direct attention to the importance of preclinical diagnosis. (Author abstract) (10 Refs)

43. SURVIVAL OF COLORECTAL CANCER PATIENTS IN RELATION TO DURATION OF SYMPTOMS AND OTHER PROGNOSTIC FACTORS.

Polissar L, Sim D, Phil M, Francis A
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Dis Colon Rectum; 24(5):364-369 1981

The effect of duration of symptoms and other prognostic factors on survival was studied by interview using a population-based sample of 154 colorectal cancer patients. The authors found that symptom durations of up to approx 1 yr before diagnosis had no effect on survival. In addition, it was found that the total number of symptoms was a statistically significant predictor of survival, although no single symptom had a significant effect. Stage, sex, and site also were found to be significant predictors of survival, whereas age, socioeconomic status, and other factors were not predictive. (Author abstract) (33 Refs)

44. THE SYNCHRONIC COLORECTAL TUMORS.

Baldizan J, Estefan A, Gateno N, Rompani O, Navarro T
Clinica Quirurgica '3'. Hospital Maciel, Fac. de Medicina, Ariosio 260, Montevideo, Uruguay
Cir Urug; 51(2):115-118 1981

The different statistics show 0.6-9.1 av 4.5% synchronic colorectal lesions of the total colon tumor cases. The wide range is due to the difference in approach. Since the new criteria were established in 1932 the percentages had increased. Five cases 54-71 yr with two or more colon lesions were presented. The problems of diagnosis and surgical treatment are discussed. The importance of radiology and colonoscopy in the diagnosis and the post surgical control and follow-up are stressed. The types of surgery to be used in the different locations of the synchronic colorectal tumors are discussed. The authors prefer one subtotal resection, if necessary to the segmented resections. During surgery a thorough examination by palpation of the whole colon should be done in the case of single or synchronic lesions to ascertain, if any additional lesions are present. The prognosis in the synchronic lesions deteriorates due to more extensive resections and usually more advanced age. (12 Refs) (In SPA)

45. EARLY POSTOPERATIVE JEJUNAL FEEDING OF ELEMENTAL DIET IN GASTROINTESTINAL SURGERY.

Ryan JA, Page CP, Babcock L
Mason Clinic, 1100 Ninth Ave., Seattle, WA, 98101
Am Surg; 47(9):393-403 1981

Gastric and colonic ileus after major abdominal operation precludes normal oral nutrition in the immediate postoperative period. Since small bowel motility and absorptive capacity are present immediately after operation, the small bowel may be used for feeding. We prospectively evaluated the efficacy of early postoperative jejunal feeding of elemental diet in three groups of patients. Fourteen adults undergoing elective partial colectomy were randomized to receive jejunal feeding of elemental diet (ED) or isotonic iv infusions of dextrose (IV). Considering all avenues of nutrition for the first 10 postoperative days, seven ED patients received a mean daily input of 2,283 cal and 14.1 g of nitrogen compared to 800 cal and 3.4 g of nitrogen for the seven IV controls (p less than 0.005). The ED patients lost 2.4% of their body wt during the first postoperative mo compared to a 6.1% wt loss for the iv controls (p less than 0.005). The ED group required an iv catheter for 1.8 days, compared to 6.6 days for the IV group (p less than 0.005). Twenty consecutive patients subjected to major upper gastrointestinal operations received a daily mean of 1,468 cal and 9.7 g of nitrogen jejunally during the 1st 10 postoperative days. Mean wt loss at 2 and 4 wk, postoperatively was 2.8% and 3.5% of preoperative wt. Ten patients received jejunal elemental diet for longer than 1 mo because of postoperative complications or adjunctive therapy for cancer. Mean wt loss was 2.8%. Early postoperative jejunal feeding of elemental diet supplies more nutrients and results in less wt loss than does iv therapy with isotonic dextrose. Early postoperative feeding is of value in patients undergoing major operations on the upper gastrointestinal tract. (Author abstract) (34 Refs)

46. TOTAL PARENTERAL NUTRITION (TPN) IN ONCOLOGY.

Wesdorp RI, Krause R, Soeters PB, Greep JM
Afdeling Algemene Heelkunde, Rijksuniversiteit, Maastricht, The Netherlands
Acta Chir Belg; 80(2/3):113-117 1981

Animal experiments and clinical trials concerning TPN are reviewed. Anorexia and cachexia in cancer patients is due to metabolic changes caused by the tumor and to its role as a nitrogen trap. If the tumor wt to body wt ratio remains low, hyperalimentation is not to the detriment of the host. Significantly increased response rate to chemotherapy with 5-fluorouracil was found in patients with colon carcinoma who received TPN before and during chemotherapy, but other trials failed to corroborate these findings. The role played by TPN has not yet been fully clarified in spite of favorable reports. Selected cachectic patients are certainly helped by TPN during therapy. Their nutritional status improves, their endurance to therapy is enhanced, and complications and side-effects are less frequent. What is even more important, there is an improvement in the quality of life. However, the survival is not prolonged by parenteral nutrition. Anorexia in cancer patiens may be altered by serotonin antagonists. (10 Refs) (In DUT)

47. INTRAMURAL EXTRAVASATION OF BARIUM SIMULATING CARCINOMA OF THE RECTUM.

Phelps JE, Sanowski RA, Kozarek RA
(c/o Sanowski), Veterans Admin. Medical Center, 7th St. and Indian School Rood, Phoenix, AZ, 85012
Dis Colon Rectum; 24(5):388-390 1981

This report describes two patients found to have barium granuloma of the rectum. The lesions appeared as indurated, ulcerated rectal masses that resembled carcinoma on endoscopic examination. Deep mucosal biopsy results demonstrated no malignancy and barium sulfate crystals in tissue macrophages. Radiographs showed persistent soft-tissue barium in the rectum. Past reports of barium granuloma have described ulcerated or polypoid masses in the rectum and anus. Rectal intramural extravasation of barium occurs as a result of asymmetric enema balloon inflation and impaction of the enema tip against the rectal mucosa. (Author abstract) (19 Refs)

48. LEIOMYOMA OF MECKEL'S DIVERTICULUM ASSOCIATED WITH ADENOCARCINOMA OF THE DESCENDING COLON.

Pujari BD, Pujari MB, Deodhare SG
Shree Hosp., Extension Area, Miraj, 416 410, India
Int Surg; 66(2):175-176 1981

A case of leiomyoma of Meckel's diverticulum associated with a carcinoma of the descending colon, presenting with intestinal obstruction, is described. Only two cases of smooth muscle tumors of the small intestine associated with carcinoma of the large bowel have been described so far, and ours is probably the first case of its kind to be reported. The importance of angiography and a thorough intraoperative exploration is stressed. (Author abstract) (5 Refs)

49. INTESTINAL LEIOMYOSARCOMA IN CHILDHOOD - CASE REPORT AND REVIEW OF THE LITERATURE.

Angerpointner TA, Weitz H, Haas RJ, Hecker WCh
(c/o Hecker) Dept. Pediatric Surgery, Univ. Children's Hosp., Lindwurmstr, 4, D-8000, Munchen, 2, W. Germany
J Pediatr Surg; 16(4,Suppl1):491-495 1981

A 4-yr-old boy with a leiomyosarcoma of the ascending colon was treated at our hospital. A multimodal therapeutical procedure consisting of both surgery and adjuvant chemotherapy was employed. The 14 previously published cases of intestinal leiomyosarcoma in childhood are reviewed. (Author abstract) (24 Refs)

50. 1-DEAZA-7,8-DIHYDROPTERIDINES, A NEW CLASS OF MITOTIC INHIBITORS WITH ANTICANCER ACTIVITY.

Wheeler GP, Bowdor BJ, Werline JA, Temple C
Kettering-Meyer Lab., Southwestern Res. Inst., Birmingham, AL, 35255
Biochem Pharmacol; 30(16):2381-2384 1981

Ethyl 5-amino-1,2-dihydro-3-[(N-methylanilino)methyl] pyrido[3,4-b]pyrazin-7-ylcarbamate (NSC-181928), a 1-deaza-7,8-dihydropteridine, was tested for its ability to cause the arrest of cultured tumor cells in mitosis. The drug was added to 24-hr-old cultures of leukemia 1210 cells, leukemia P388/0, cells and vincristine-resistant P388/VCR cells and to 48-or 72-hr-old cultures of other cell lines including plastic-attached cultures of murine colon tumors number 26 (ip implanted) and number 38 (sc implanted). The cells were harvested at selected times, washed, and used for the preparation of microscopic slides. After the slides were stained with toluidine blue, 1,000 cells/slide were counted and classified as interphase or mitotic. NSC-181928 was active against all cell lines tested. Its effect was quantitatively similar to that of VCR and vinblastine (VB) for P388/0, colon tumor number 26 cells, and colon tumor number 38 cells. Its activity against P388/VCR was similar to that of VB and similar to its activity against P388/0. These results demonstrated that NSC-181926 can prevent the progression of cells through mitosis. (16 Refs)

51. THE EFFECTS OF NANDROLONE DECANOATE (ND) ON THE TOXICITY AND ANTI-TUMOUR ACTION OF 1-(2-CHLOROETHYL)-3 CYCLOHEXYL-1-NITROSOUREA (CCNU) AND 5 FLUOROURACIL (5FU) IN EXPERIMENTAL MURINE COLON TUMOURS.

Bibby MC, Double JA, Mughal M
Sch. Medical and Surgical Sciences, Univ. Bradford, Bradford, England
Br J Pharmacol; 74(1):295p 1981

A clinical impression that pretreatment with high doses of anabolic steroids reduces the toxicity of various cytotoxic agents was tested using mouse adenocarcinoma of the colon (MAC) as model. In normal 6-8 wk old NMRI mice the LD50 values for single ip injections of 1-(2-chloroethyl)-3 cyclohexyl-1-nitrosourea (CCNU) and 5 fluorouracil (5FU) were respectively 80 and 180 mg/kg. Groups of mice were injected with 50 mg/kg nandrolone decanoate (ND) on day 0 and received cytotoxic drugs at intervals afterwards. For CCNU the LD50 value increased by 50% to 120 mg/kg by day 7; for 5FU it rose by 83% to 300 mg/kg on day 10. While simultaneous administration of ND did not affect toxicity or anti-tumor action of either agent, seven-day pretreatment increased the LD50 value of CCNU 43% from 77 to 110 mg/kg without reducing its anti-tumor activity against MAC 13. Similar effects were seen for 5FU against MAC 26; the LD50 rose 79% from 180 to 295 mg/kg. Administration of ND resulted in a sharp rise in peripheral WBC count lasting at least 30 days; pretreatment maintained the WBC count in the presence of CCNU at control levels, even though CCNU produces a WBC reduction in both ND- and non-ND-treated groups. Because CCNU and 5FU are widely used in the management of metastatic cancer, clinical repetition of these results would represent a significant improvement in cancer chemotherapy. (2 Refs)

52. EFFECTS OF CYCLIC-NUCLEOTIDE DERIVATIVES ON THE GROWTH OF HUMAN COLONIC CARCINOMA XENOGRAFTS AND ON CELL PRODUCTION IN THE RAT COLONIC CRYPT EPITHELIUM.

Tutton PJ, Barkla DH
Dept. Anatomy, Faculty Medicine, Monash Univ., Clayton, Victoria 3168, Australia
Br J Cancer; 44(2):182-188 1981

Previous studies have shown that various amine hormones are able to influence the growth rate of human colorectal carcinomas propagated as xenografts in immune-deprived mice, and it is now well known that the effects of many amine and other hormones are mediated by cyclic nucleotides, acting as second messengers within cells. In the present study the influence of various derivatives of cyclic AMP and cyclic guanosine monophosphate on the growth of two different lines of colorectal cancer growing in immune-deprived mice, and on the cell production rate in the colonic crypt epithelium of the rat, was assesssed. Growth of each tumor line, as well as crypt-cell production, was suppressed by treatment with N6O2' dibutyryl and N6 monobutyryl derivatives of cyclic AMP. Dibutyryl cyclic guanosine monophosphate, on the other hand, was found to promote the growth of Tumor HXK4 and to promote crypt cell production, but to have no significant effect on Tumor HXM2. (Author abstract) (35 Refs)

53. ALKALINE PHOSPHATASE IN HT-29, A HUMAN COLON CANCER CELL LINE: INFLUENCE OF SODIUM BUTYRATE AND HYPEROSMOLALITY.

Herz F, Schermer A, Halwer M, Bogart LH
Dept. Pathology, Montefiore Hosp. and Medical Center, Bronx, NY, 10467
Arch Biochem Biophys; 210(2):581-591 1981

A number of gene loci in humans encode the different forms of alkaline phosphatase; at least one codes for the intestinal form. The cell line HT-29 (derived from a human adenocarcinoma of the colon) exhibits a very low alkaline phosphatase activity; the enzyme isolated from these cells is of the intestinal type and is thermolabile in the presence of 2-amino-2-methyl-1-propanol-HCl buffer. Hyperosmolality of the culture medium and/or the presence of sodium butyrate induced increased levels of activity; specific activity rose 1,000-fold in the presence of both conditions. The effect of hyperosmolality was blocked by cycloheximide (2 and 10 uM) and of sodium butyrate by thymidine (2 and 10 milliM). This human cancer cell line is unique because the enzyme of HT-29 is not affected by cell density or by glucocorticoid hormones. 5-Bromo-2'-deoxyuridine and inhibitors of DNA synthesis caused a slight decrease in specific activity. When the enzyme was tested against various inhibitors, there was a linear relationship between the reciprocal of the reaction velocity and the inhibitor concentration. These results represent the first report in which the synthesis and modulation of the intestinal form of alkaline phosphatase has been documented in a cell line derived from a human colon adenocarcinoma. (64 Refs)

54. EFFECTS OF 12-O-TETRADECANOYL PHORBOL-13-ACETATE AND EPIDERMAL GROWTH FACTOR ON THE PROLIFERATION OF HUMAN MUTANT FIBROPLASTS IN VITRO.

Gansler T, Kopelovich L
(c/o Kopelovich), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Lett; 13(4):315-323 1981

The role of cell density in the response of cultured skin fibroblasts (SF) from individuals with hereditary adenomatosis of the colon and rectum (ACR) and from normal individuals to 12-O-tetradecanoyl phorbol-13-acetate (TPA) and to epidermal growth factor (EGF) was examined. The effect of TPA and EGF on the morphology of cell clones was also studied. Treatment of high density (6 x 10(4) cells/square cm) ACR-SF cultures with TPA produced dose-dependent stimulation of cell proliferation over the entire (0.5-100 nanog/ml) range tested. Addition of TPA to sparse (4.75 x 10(3) cells/square cm) cultures resulted in biphasic dose-response, with max inhibition at 2.0-10 nanog/ml. Similar results were found with normal human SF, primarily in sparse cultures, but these cells were more sensitive than ACR-SF. Normal SF in dense culture were not responsive to TPA stimulation. EGF (0.01-10 nanog/ml) was mitogenic in both sparse and confluent ACR-SF cultures in a dose-dependent manner. At EGF levels above 50 nanog/ml, however, inhibition of cell proliferation became apparent. Normal SF responded similarly. TPA exposure induced formation of dendritic-like cells with irregular thin cytoplasmic processes in both cell types. ACR-SF exposed to EGF were more densely packed and spindle-shaped, with more parallel orientation in the periphery. The results suggested that EGF and TPA share one of two existing TPA receptors; the higher affinity (unshared) receptor becomes saturated at ligand concentrations below 10 nanog/ml. TPA inhibition in sparse culture reflects the extent of neoplastic transformation; the less sensitive tumor cells apparently lack the higher affinity receptors. (26 Refs)

55. THREE DIFFERENT HUMAN TUMOR CELL LINES CONTAIN DIFFERENT ONCOGENES.

Murray MJ, Shilo BZ, Shih C, Cowing D, Hsu HW, Weinberg RA
Center Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cell; 25(2):355-361 1981

We have obtained foci of transformed mouse cells after transfection of human DNA from colon and bladder carcinoma cell lines and a promyelocytic leukemia cell line. These foci can be shown to contain a large number of human DNA sequences by use of highly repetitive human DNA sequence probes. Cell DNA from primary foci can be used in a subsequent cycle of transfection resulting in secondary foci that contain relatively little human DNA. Secondary foci appear to contain only the human sequences proximal to those responsible for the transformed phenotype. A set of characteristic DNA restriction fragments is found in common among secondary foci derived from each tumor cell line DNA. Comparison of the common DNA fragments found in secondary foci derived from three different human tumor cell lines indicates that these three cell lines contain three different transforming genes. (Author abstract) (32 Refs)

56. CONSISTENT MOLECULAR GENETIC VARIATION IN HUMAN GASTROINTESTINAL CARCINOMAS.

Humphries P
Dept. Medical Genetics, Medical Biology Centre, Queen's Univ. Belfast, 97 Lisburn Road, Belfast BT9 7BL, Northern Ireland
Nature; 293(5828):146-148 1981

DNA sequences in five human gastrointestinal carcinomas were analyzed by autoradiographic scanning after hybridization to recombinant DNA. The DNA was digested with EcoRI restriction endonuclease, separated by electrophoresis in agarose gel, then blot-transferred and hybridized to P32-labeled DNA probes derived from the 14-or 50-kilobase (kb) regions. Hybridization signals produced by two moderately differentiated sigmoid tumors, a moderately differentiated rectal tumor, an invasive stomach tumor, and a colon tumor are described. Results demonstrated that a consistent genetic variation underlies that apparently random degeneration detected at the chromosome level in advanced human carcinomas. The tendency for hybridization signals to disappear may reflect loss of DNA sequences or their relocation to different sites in the genome. (18 Refs)

57. S-PHASE FRACTIONS OF COLORECTAL CARCINOMAS RELATED TO PATHOLOGIC AND CLINICAL FEATURES.

Meyer JS, Prioleau PG
Dept. Pathology, Jewish Hosp., 216 S. Kingshighway, P.O. Box 14109, St. Louis, MO, 63178
Cancer; 48(5):1221-1228 1981

The S-phase fractions (SPFs) of epithelial cells in 100 resected colorectal carcinomas were measured by in vitro exposure to tritiated thymidine and autoradiography. The frequency distribution of SPFs was gaussian with a median of 17.8 per hundred in 90 unirradiated carcinomas, whereas in 10 carcinomas given radiation therapy preoperatively, it was positively skewed with a median of 6.9. Analysis of the unirradiated carcinomas showed no relationship between SPF and various clinical and morphologic features that included age, race, sex, site, size, Dukes' stage, histologic grade of the tumor, number of metastasis-bearing regional lymph nodes, presence of adenomas of the large bowel, survival or relapse-free survival of the patient, or SPF or adjacent normal colorectal crypts. The results show no evidence that colorectal carcinomas can be divided into kinetic subsets. The spatial orientation of labeled cells in autoradiographs indicated presence of a nonproliferative fraction of cells in many tumors that may modulate response to radiation therapy and chemotherapy. (Author abstract) (47 Refs)

58. KINETICS OF THE NON-NEOPLASTIC MUCOSA OF THE LARGE BOWEL OF DIMETHYLHYDRAZINE-TREATED RATS.

Sunter JP, Watson AJ, Appleton DR
Dept. Pathology, Queen Elizabeth Hosp., Gateshead, Tyne and Wear, NE9 6SX, England
Br J Cancer; 44(1):35-44 1981

Administration of 1,2 dimethylhydrazine (DMH) to rats by weekly sc injections causes the development of multiple epithelial tumors of the large bowel. These appear to arise as localized dysplastic abnormalities in hitherto apparently morphologically normal crypts. This study was undertaken in order to examine cell proliferation in such apparently normal crypts of DMH-treated animals. A number of proliferative abnormalities are evident, including changes in the size of the crypts, changes in the disposition of proliferating cells within them and reduced cell-cycle times. The nature and the extent of the abnormalities vary from site to site along the length of the bowel, and reflect the vulnerability of the different segments of the bowel, not only to the carcinogenic effects of DMH, but also to short-term toxicity. (Author abstract) (23 Refs)

59. ALTERATIONS IN SURFACE ULTRASTRUCTURE AND ANIONIC SITES OF RAT DIMETHYLHYDRAZINE-INDUCED INTESTINAL TUMORS.

Jacobs LR
Dept. Internal Medicine, Sch. Medicine, TB 192, Univ. California, Davis, CA, 956 16
Virchows Arch [Cell Pathol]; 37(2):207-216 1981

The relative roles of cell surface shedding and electronegative charge as determinants of metastatic capacity were studied in experimentally produced intestinal tumors. The ultrastructural organization and distribution of anionic sites on the luminal plasma membrane surface components were examined in small intestinal and colonic tumors induced in male Sprague-Dawley rats with 1,2-dimethylhydrazine. The overall distribution of negatively charged groups was demonstrated with ruthenium red staining. Compared to normal epithelial cells, neoplastic cells revealed evidence of decreased cell surface shedding as manifested by decreased numbers of membrane-bound bodies, and an increased quantity of glycocalyx. Malignant cell surfaces were directly exposed to the intestinal lumen as a result of losing the enteric surface coat covering. The exposed microvilli appeared damaged with shortening and blunting. The glycocalyx and surface coat both reacted strongly with ruthenium red indicating the presence of anionic sites. As a result of surface coat loss, the malignant cell surface components revealed an overall decrease in net negative charge. These alterations in cell surface component ultrastructure and electronegative charge appear to be consistent with the low capacity for chemically induced rat intestinal tumors to metastasize. (Author abstract) (15 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

60. DOES PEUTZ-JEGHERS SYNDROME PREDISPOSE TO GASTROINTESTINAL MALIGNANCY? A LATER LOOK.

Linos DA, Dozois RR, Dahlin DC, Bartholomew LG
(c/o Dozois) Dept. Surgery, Mayo Clinic, Rochester, MN, 55905
Arch Surg; 116(9):1182-1184 1981

Several reports have recently suggested an association between the development of intestinal carcinoma and the presence of Peutz-Jeghers syndrome. During the 45-yr period between 1935 and 1979, 48 patients with Peutz-Jeghers syndrome were seen at the Mayo Clinic, Rochester, Minnesota, and followed up for a median period of 33 yr. Carcinoma of the small or large intestine did not develop in any patient, with possibly one exception. Survival of patients with Peutz-Jeghers syndrome also was found to be similar to that of the general population. Therefore, skepticism continues about the premalignant potential of this rare syndrome, especially in the small intestine, and surgical conservatism should be practiced in its management. (Author abstract) (18 Refs)

61. CARCINOMA OF THE RECTUM IN MALE HOMOSEXUALS.

Leach RD, Ellis H
Surgical Unit, Westminster Hosp., London SW1P 2AP, England
J R Soc Med; 74(7):490-491 1981

Two male homosexuals with carcinomata of the rectum with transitional cell changes are reported, and the possible etiology of these lesions is discussed. (Author abstract) (4 Refs)

62. CHOLECYSTECTOMY AND RIGHT-SIDED COLON CANCER: AN EPIDEMIOLOGICAL STUDY.

Vernick LJ, Kuller LH
(c/o Kuller) Dept. Epidemiology, Graduate Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA
Lancet; 2(8243):381-383 1981

The relation between prior cholecystectomy and right-sided colon cancer was investigated in a case-control study of 150 patients with histologically confirmed adenocarcinoma of the cecum or ascending colon and of two comparison groups. One comparison group consisted of 150 patients, matched for age, sex, and race, who had histologically confirmed adenocarcinoma of the descending or sigmoid colon and the other of 123 neighborhood controls. Compared with left-sided cancer controls, the right-sided colon cancer cases had a relative risk of 1.87 for colon cancer after cholecystectomy. The relative risk was 1.86 when they were compared with the neighborhood controls. When compared with both control groups relative risk was 1.77, with 95% confidence limits of 0.95 and 3.3 ($p = 0.07$). The increased risk of right-sided colon cancer after cholecystectomy may be associated with changes in biliary metabolism occurring after removal of a gall bladder. (Author abstract) (18 Refs)

63. CHOLECYSTECTOMY AND CANCER OF THE LARGE BOWEL.

Turnbull PR, Smith AH, Isbister WH
(c/o Isbister) Dept. Surgery, Wellington Clinical Sch. Medicine, Wellington, New Zealand
Br J Surg; 68(8):551-553 1981

A matched case control study was conducted in order to determine the association between previous cholecystectomy and the development of large bowel cancer. One hundred and sixty men and 145 women presenting with large bowel cancer were studied. One control was selected for each case matched according to age, sex and date of admission. The medical records for each patient in the study were reviewed for evidence of previous cholecystectomy. No association was found among male patients, but for women an estimate of relative risk of 2.7 was obtained for patients who had had previous cholecystectomy. This association was largely a consequence of the fact that 10 female patients with rectal cancer had had a previous cholecystectomy compared with only 1 of their controls. It is possible that carcinogenic breakdown products of bile salts are most concentrated in the distal portion of the large bowel, but it is difficult to explain why the association should be confined to women only. (Author abstract) (24 Refs)

64. CHOLECYSTECTOMY AND CARCINOMA OF THE COLON.

Linos DA, O'Fallon WM, Beart RW, Beard CM, Dockerty MB, Kurland LT
Section Publications, Mayo Clinic, Rochester, MN, 55905
Lancet; 2(8243):379-381 1981

After cholecystectomy the concentration of secondary bile acids in the bile increases. These bile acids have been incriminated in the pathogenesis of carcinoma of the colon. Hence the hypothesis that cholecystectomy predisposes to the development of carcinoma of the colon. To test this hypothesis, 1,681 residents of Rochester, Minnesota (460 males and 1,221 females), who underwent cholecystectomy during 1950-69, were followed up. Carcinoma of the colon developed in a higher-than-expected number of patients. However, the association was significant only in females (relative risk 1.7; 95% confidence interval 1.1-2.5) and even stronger for right-sided carcinoma of the colon (relative risk 2.1; 95% confidence interval 1.1-3.6). These data support the hypothesis that cholecystectomy may be a predisposing factor in the development of cancer of the colon in women. (Author abstract) (20 Refs)

65. AN EPIDEMIOLOGICAL SURVEY OF EIGHT OIL REFINERIES IN BRITAIN.

Rushton L, Alderson MR
Div. Epidemiology, Inst. Cancer Res., Sutton, Surrey SM2 5PX, England
Br J Ind Med; 38(3):225-234 1981

A mortality study of workers employed for at least 1 yr between 1 January 1950 and 31 December 1975 at eight oil refineries in Britain has been carried out. Over 99% of the population were successfully traced to determine their vital status at 31 December 1975. The mortality observed in the study population was compared with that which would be expected from the mortality rates for the all male population of England and

Wales, and Scotland, with adjustment for regional variation in mortality for the English and Welsh refineries. The overall mortality observed was considerably lower than that expected on this basis, as was the mortality from heart disease, stroke, bronchitis, and pneumonia. The observed number of deaths from all neoplasms was also very much less than expected, a result almost entirely due to a large deficit of observed deaths from lung cancer. Raised mortality patterns were found in several refineries for cancers of the esophagus, stomach, intestines, and rectum, although no location was consistently high for all these causes of death. Different yr-of-entry cohorts and job groups were also affected. In general, mortality from these causes increased as length of service and interval from starting work increased. There were also significantly more observed deaths than expected from cancer of the nasal cavities and sinus, and melanoma. Further work is required to ascertain whether these are due to an occupational factor and, if so, to identify the physical or chemical nature of the risk. (Author abstract) (32 Refs)

66. COMPOSITION OF FECAL BILE ACIDS AND NEUTRAL LIPIDS IN JAPANESE PATIENTS WITH LARGE BOWEL CANCER AND NORMAL CONTROLS.

Sasaki T
First Dept. Surgery, Tottori Univ., Sch. Medicine, Yonago-shi, Tottori Pref. 683, Japan
Yonago Igaku Zasshi; 32(2):115-130 1981

Since bile acids and neutral lipids have a potential significance in the pathogenesis of colon cancer, fecal bile acids and neutral lipids in feces were analyzed in Japanese patients with large bowel cancer and normal controls. Seventeen kinds of fecal bile acids were found in the patients with colon cancer or rectal cancer. Sixteen of the 17 fecal bile acids were also found in the normal controls, but 3alpha-hydroxy-6-ketocholanoic acid was not found in this group. Three kinds of fecal bile acids, 3alpha-hydroxy-6-ketocholanoic acid, 7beta-hydroxy-3-ketocholanoic acid, and 3,7-diketocholanoic acid were newly found in this study. The concentration of total bile acids in feces was 5.19 mg in normal controls, 5.22 mg in patients with colon cancer, and 4.23 mg in patients with rectal cancer. No statistical difference was found in the concentrations of bile acids between the patients with large bowel cancer and normal controls. An increase in the concentration of fecal primary bile acids, especially chenodeoxycholic acid, was found in patients with colon cancer compared with normal controls and patients with rectal cancer. The level of primary bile acids in total bile acids was higher in patients with colon cancer or rectal cancer than in normal controls. The level of secondary fecal bile acids in total bile acids was lower in patients with colon cancer or rectal cancer than in normal controls. However, no statistical difference was observed between the two cancer groups and normal controls. The concentration of keto bile acids and the level of keto bile acids in total bile acids were significantly lower in patients with colon cancer or rectal cancer than in normal controls. The concentrations of total neutral lipids, coprostanol, cholesterol, and other sterols and coprostanol/cholesterol ratios between the patients with large bowel cancer and normal controls were not significantly different. (Author abstract) (35 Refs) (In JPN)

67. THE ROLE OF N-NITROSAMINE IN CARCINOGENESIS AT THE URETEROCOLIC ANASTOMOSIS.

Stewart M, Hill MJ, Pugh RC, Williams JP
St. Paul's Hosp., 24 Endell St., London WC2H 9AE, England
Br J Urol; 53(2):115-118 1981

Seven cases of colonic tumors occurring at the ureterocolic anastomosis (UCA) in patients diverted for benign disease are presented and comparisons made with existing literature. There appears to be a definite increase in the incidence of colonic malignancy in patients with this diversion. A theory of carcinogenesis involving bacterial activation of endogenously formed N-nitrosamine is suggested. Preliminary results of rectal urine analysis support this theory in that high concentrations of N-nitrosamine have been found and mutagens demonstrated. (Author abstract) (10 Refs)

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COLO-RECTAL CANCERS

Diagnosis, Treatment

SERIES CT07 No. 82/02

FEBRUARY, 1982

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. HEMOCCULT II TEST. ROUTINE SCREENING PROCEDURE FOR COLORECTAL NEOPLASM?

Stuart M, Killingback MJ, Sakker S, Failes DG, Frost GW, Mennie B
Sydney Hosp., 231 Macquarie St., Sydney, New South Wales 2000, Australia

Med J Aust; 1(12):629-631 1981

In October, 1978, the Hemoccult II Test was introduced as a screening procedure by the Sydney Hospital Health Information and Screening Service. In the first 2 yr, 4,498 people were screened and 150 positive results were obtained. These people were referred for further investigation, with 114 choosing to attend the Edward Wilson Colon and Rectum Unit outpatient clinic at Sydney Hospital. Forty-four patients were found to have 59 colorectal neoplasms of which 13 were carcinomas. This represents a cancer incidence of 0.29% and corroborates the results of similar studies conducted overseas. (Author abstract) (13 Refs)

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HE 20.3173/2:

2. A RANDOMISED TRIAL TO INVESTIGATE X-PREP, ORAL MANNITOL AND COLONIC WASHOUT FOR DOUBLE-CONTRAST BARIUM ENEMA.

Lee JR, Hares MM, Keighley MR
General Hosp., Birmingham, England
Clin Radiol; 32(5):591-594 1981

Three methods of bowel preparation used prior to double contrast barium enemas were compared by a randomized trial in 60 patients. Evaluation was by radiological review and from a patient questionnaire. The preparations included X-Prep liquid with colonic washout, oral mannitol alone and oral mannitol with colonic washout. Adequacy of preparation as judged by fecal residue was significantly better after X-Prep than in either group receiving mannitol. The more severe purgation with mannitol did not result in better clearance of the large bowel and the addition of a colonic washout to mannitol did not reduce fecal residue. Side-effects and adverse comments were more common after mannitol. Diarrhea was significantly less after X-Prep than after mannitol. (Author abstract) (13 Refs)

3. PRE-OPERATIVE COMPUTED TOMOGRAPHY OF CARCINOMA OF THE RECTUM.

Dixon AK, Fry IK
Univ. Dept. Radiology, Addenbrooke's Hosp., Hills Road, Cambridge CB2 2QQ, England
Br J Radiol; 54(644):655-659 1981

Fifty-two patients with carcinoma of the rectum underwent computed tomography (CT) in the immediate preoperative period. CT was used in order to assess extrarectal tumor spread. The resected specimen was staged by the pathologist who subdivided spread in continuity beyond the bowel wall into slight, moderate or extensive. In 21 out of 23 patients with no or slight extrarectal local spread CT showed normal perirectal fat. Extrarectal spread was demonstrated by CT in eight of the nine patients found to have extensive local spread. This was seen to be circumferential in the only two patients with inoperable tumors. CT identified discrete nodal enlargement in 7 of the 18 patients with histologically involved lymph nodes. CT may help the less experienced surgeon, especially when he is not confident of his findings at digital examination. CT allows assessment of high rectal tumors which cannot be examined digitally. It may play a role where a tumor with extensive local spread is clinically suspected and confirmation is needed before preoperative radiotherapy is given. (Author abstract) (3 Refs)

4. DETECTION AND STAGING OF PRIMARY RECTAL AND RECTOSIGMOID CANCER BY COMPUTED TOMOGRAPHY.

Thoeni RF, Moss AA, Schnyder P, Margulis AR
Dept. Radiology, M-396, Univ. California, San Francisco, CA, 94143
Radiology; 141(1):135-138 1981

Thirty-nine patients were examined by computed tomography (CT) prior to resection of primary rectal [23] or rectosigmoid carcinoma [16]. There were 3 patients in Stage II [thickened bowel (greater than 0.5 cm) alone], 12 in Stage IIIa (thickened bowel wall and invasion of adjacent tissue, muscles, or organs, but no extension to the pelvic side walls), 18 in Stage IIIb (extension to the pelvic side walls), 6 in Stage IV (pelvic tumor and distant metastases), and none in Stage I (intraluminal mass without wall thickening). CT detected all 39 rectal or rectosigmoid tumors (sensitivity = 100%) and had an overall staging accuracy of 92%. These results show that CT is useful and accurate in detecting and staging primary rectal and rectosigmoid tumors. (Author abstract) (11 Refs)

5. THE PROGNOSTIC SIGNIFICANCE OF SPECIFIC HISTOLOGIC FEATURES OF CARCINOMA OF THE COLON AND RECTUM.

de Mascarel A, Coindre JM, De Mascarel I, Trojani M, Maree D, Hoerni B
Fondation Bergonie, Bordeaux, France
Surg Gynecol Obstet; 153(4):511-514 1981

The prognostic significance of several histologic features of the primary tumors and regional lymph nodes was analyzed in 82 consecutive patients with carcinoma of the colon and rectum. Three criteria were shown to have a statistically significant favorable impact on prognosis: Dukes' A or B stages, the absence of mucinous components and the presence of lymphoplasmocytic infiltration in or around the tumor. Based upon the number of these criteria present, we were able to separate the patients into three distinct prognostic groups. We suggest that such a grouping is simple and should be considered in the design and analysis of future adjuvant trials done for carcinoma of the colon and rectum. (Author abstract) (7 Refs)

6. IMMUNOPEROXIDASE LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL HUMAN INTESTINAL MUCOSA.

Primus FJ, Clark CA, Goldenberg DM
Dept. Pathology, Div. Experimental Pathology, Univ. Kentucky Coll. Medicine, MS-409, Lexington, KY, 40536
JNCI; 67(5):1031-1039 1981

The indirect, labeled antibody and peroxidase-antiperoxidase complex (PAP) methods were studied to determine their sensitivity in detecting carcinoembryonic antigen (CEA) in conventionally processed specimens of morphologically normal human colon mucosa. CEA-positive staining was demonstrated in 13 of 19 specimens reacted with the PAP method, whereas only 4 of these specimens stained positive with the labeled antibody procedure. Detection of CEA with either technique was unrelated to normal mucosa content of antigen as determined by radioimmunoassay. Tissue fixation in 95% ethanol-1% acetic acid (EA) resulted in an enhanced and defined cytoplasmic staining of the normal colon cell lining the mucosal surface and upper levels of the glandular crypts. Cytoplasmic localization in Formalin-fixed specimens was absent or markedly reduced. Colon goblet cells and the small intestinal epithelium were CEA-negative in both Formalin- and EA-fixed specimens. These results show that the PAP immunoperoxidase method is more sensitive than the indirect, labeled antibody procedure in detecting CEA in morphologically normal colon mucosa. Furthermore, staining of tissues fixed in EA demonstrated that CEA is a product of the columnar epithelial cell and is not associated with goblet cells. (Author abstract) (38 Refs)

7. HISTOCHEMICAL STUDY OF MUCIN IN THE MUCOSA ADJACENT TO COLORECTAL CARCINOMA ASSOCIATED WITH SOLITARY OR MULTIPLE ADENOMATOUS POLYPS.

Lapertosa G, Fulcheri E, Pietra A
Istituto di anatomia ed istolgia patologica, Universita di Genova, Genova, Italy
Pathologica; 73(1025):467-471 1981

Mucin scrapings from colorectal adenocarcinomas associated with adenomatous polyps from 12 patients were examined histochemically. Increased sialomucin level and reduced level or absence of sulfomucin were found in normal transition mucosa adjacent to the adenocarcinomas and adenomatous polyps showing high degree of atypia or signs of incipient malignant transformation. Even higher sialomucin levels were found near adenocarcinomas of Stage C according to Duke's classification. The sialomucin levels were elevated in the mucosa near hyperplastic polyps without potential malignancy. At a distance of 5 cm from the adenocarcinomas, both sialomucin and sulfomucin were present, at times with predominance of the latter. The findings indicate the diagnostic and prognostic significance of sialic acid in the transitional mucosa of patients with colorectal carcinoma and adenomatous polyps. (7 Refs) (In ITA)

8. PATTERNS OF MUCIN SECRETION IN NEOPLASTIC AND NON-NEOPLASTIC DISEASES OF THE COLON.

Listinsky CM, Riddell RH
Dept. Pathology, Univ. Chicago Hosp. and Clinics, Chicago, IL, 60637
Hum Pathol; 12(10):923-929 1981

Changes in the pattern of sulfomucin and sialomucin secretion and height of large bowel mucosa have been described adjacent to primary colonic adenocarcinomas and adenomas, and called 'transitional' mucosa. These changes were initially thought to be specific preneoplastic changes. In this study 'transitional' changes in colonic and rectal mucosa were found in some cases overlying benign mesenchymal tumors, metastatic tumors from noncolonic sites, and sites of endometriosis, as well as adjacent to primary colonic and rectal neoplasms. These findings suggest that although these changes may be found adjacent to primary large bowel neoplasms, they are frequently secondary reactive rather than primary preneoplastic phenomena. In addition, the thickness of the mucosa and the accompanying pattern of mucin secretion usually seen in transitional mucosa may be dissociated. (Author abstract) (13 Refs)

9. ESTROGEN AND PROGESTERONE BINDING PROTEINS IN HUMAN COLORECTAL CANCER. A PRELIMINARY CHARACTERIZATION OF ESTRADIOL RECEPTOR.

Sica V, Contieri E, Nola E, Bova R, Papaleo G, Puca GA
I. Facolta di Medicina e Chirurgia, Istituto di Patologia Generale, Via S. Andre a delle Dame 2, 80138 Napoli, Italia
Tumori; 67(4):307-314 1981

Estradiol receptor (ER) and progesterone receptor (PgR) were assayed in tumors from 20 patients with primary colorectal cancer. Ten of 20 tumors contained high affinity sites for 17beta-estradiol and progesterone. The highest concentration of ER was 56 fmol/mg of protein. The ER dissociation constant ranged from 1.6 x 10(-10) M to 8 x 10(-10) M (mean 4.6 +-2.6). The highest concentration of PgR was 42 fmol/mg of protein. The PgR dissociation constant ranged from 3 x 10(-9) to 9 x 10(-9) M (mean 5.65 +-2.1). Four out of 20 specimens analyzed were from male patients and all resulted negative for both receptors. Sixty percent of ER positive tumors were also PgR positive, whereas only 20% of ER negative were PgR positive. Sucrose gradient centrifugation showed that cytoplasmic ER of colorectal cancer sedimented at 3 S in the absence of protease inhibitors and at 4.5 S in the presence of 1 mM phenylmethylsulphonyl fluoride (PMSF) both in low and in high ionic strength. When chromatographed on Sephadex G-200 almost all ER was quantitatively recovered in the included fractions. Mol wt of ER eluted from Sephadex G-200 ranged from 90,000 to 50,000 daltons. Elution profile and mol wt heterogeneity suggest that, in spite of the presence of PMSF, there is a limited proteolysis of ER. Partially purified colorectal cancer ER did not bind to sepharose-heparin. The isoelectric point of ER was 6.4-6.5. (Author abstract) (35 Refs)

10. PLASMA CAMP AND CAMP-PHOSPHODIESTERASE (PDE) LEVELS IN CANCER PATIENTS BEFORE AND AFTER SURGERY.

Patel V, Banu N, Malhotra OP, Udupa KN
Surgical Res. Lab., Inst. Medical Sciences, Banaras Hindu Univ., Varanasi 221 005, India
Indian J Cancer; 18(3):181-184 1981

Plasma levels of cyclic AMP (cAMP) and cAMP-phosphodiesterase (PDE) were measured in 40 patients 1 wk before and 1 wk after surgery. Cases included ten each of liver, stomach, colon, and breast cancer. Ages ranged from 40 to 60 yr. Ten healthy individuals served as controls. Normal values were 19.614 +-0.722 picomoles (pmol) cAMP/ml plasma and 20.854 +-0.807 pmol PDE/ml plasma. All cancer patients studied showed decreased cAMP levels (11.016-14.216 pmol/ml) before surgery. PDE levels were increased (23.894-34.798 pmol/ml) in all patients before surgery. After surgery cAMP levels returned to normal in patients with breast, colon, or stomach cancer. Levels remained below normal (16.212 pmol/ml) in liver cancer patients. PDE levels decreased after surgery in all cases. Levels were normal in breast cancer patients, but remained higher than normal in the other groups. Failure of cAMP values for liver cancer patients to return to normal after surgery was probably due to the fact that liver tumors were not completely removed by surgery. Results suggest that abnormal proliferation of cancer cells may be explained by decreased cAMP and increased PDE levels. (27 Refs)

11. INCREASED INACTIVE CREATINE KINASE B PROTEIN IN THE PLASMA OF PATIENTS WITH MALIGNANCY.

Burnam MH, Barstis JL, Stern CS, Rose DM, Crouch MA, Haskell CM, Singh BN
Cardiology Section (691/111E), Wadsworth Veterans Admin. Medical Center, Wilshire and Sawtelle Blvd., Los Angeles, CA, 90073
Clin Chem; 27(10):1724-1728 1981

Using a specific radioimmunoassay for enzymically inactive creatine kinase (EC 2.7.3.2) B protein (CK-Bi), we studied 139 patients with various malignancies. We found it to be increased in certain adenocarcinomas, including colorectal, lung, and prostate, as has also been reported for enzymically active CK-BB. Of 15 patients with leukemia or lymphomas with active disease, 12 also had increased values for CK-Bi in plasma. In these patients, concentrations of CK-Bi in plasma tended to correlate with disease activity, increasing with aggressive malignancy and decreasing on successful treatment. Thus, measurement of CK-Bi may constitute a sensitive means for detecting malignancy and, in certain subsets of patients, for monitoring therapeutic response. (Author abstract) (15 Refs)

12. CHROMOSOMAL BANDING PATTERNS IN HUMAN LARGE BOWEL CANCER.

Reichmann A, Martin P, Levin B
Dept. Medicine, Section Gastroenterology, Univ. Chicago, Box 400, 950 East 59th St., Chicago, IL, 60637
Int J Cancer; 28(4):431-440 1981

Cytogenetic banding studies were performed on direct preparations from 31 large bowel tumors. Twenty-eight of these were from primary sites and three from metastases. Some distinctive patterns were observed. The 31 tumors were separable into four groups: (1) Tumors with normal karyotypes (3 cases); (2) tumors with simple gains of chromosomes (3 cases); (3) tumors with gains, losses and structural aberrations (10 cases). Groups 1, 2 and 3 were all in the diploid range; and (4) tumors with hypotriploid-hypotetraploid karyotypes (15 cases). Non-random gains of several chromosomes, especially Number 8 and non-random losses of Number 17 were seen in this series. Thirteen cases had sex chromosome abnormalities. The most prominent structural abnormalities involved chromosomes Number 1 and Number 5. Marker chromosomes were sometimes absent, but when present ranged from simple translocations to the most complex rearrangements. Doubling of chromosome and/or marker chromosomes were prominent in Group 4. Double minutes were seen in all three metastatic tumors and three primary cancers. Premature chromosome condensation was observed in three cases in the hypotriploid-hypotetraploid group. (Author abstract) (40 Refs)

13. OCCURRENCE OF IN VITRO TETRAPLOIDY IN THE HERITABLE COLON CANCER SYNDROMES.

Danes BS
New York Hosp.-Cornell Medical Center, 525 E. 68th St., New York, NY, 10021
Cancer; 48(7):1596-1601 1981

Increased in vitro tetraploidy occurred in skin cultures derived from all affected patients and some family members at risk studied in families with heritable colon cancer syndromes (15 of 16 Gardner syndrome families, three Oldfield syndrome families, and four families with heritable colon cancer syndrome without polyposis coli) but was not present in all (one Gardner syndrome family, 16 of 19 familial polyposis coli families, and two Turcot syndrome families). Seven of 97 controls, family members by marriage, showed increased in vitro tetraploidy. None of these seven had a family history of colonic cancer but four had a family history of other solid tumors. Such in vitro studies illustrated that the occurrence of in vitro tetraploidy should be determined in families rather than individuals in order to determine whether all patients clinically affected show increased in vitro tetraploidy and vertical transmission that can be documented. (Author abstract) (21 Refs)

14. EARLY CARCINOMA AND ADENOMA OF THE LARGE INTESTINE: USEFULNESS OF FECAL OCCULT BLOOD TESTING FOR DETECTION AND FACTORS RELATING TO BLEEDING.

Yoshii Y, Kobayashi S, Kuroda T, Kasugai T
First Dept. Internal Medicine, Aichi Cancer Center Hosp., Chikusa-ku, Nagoya 464, Japan
Nippon Daicho Komonbyo Gakkai Zasshi; 34(3):220-223 1981

From January 1976 to May 1980, patients presenting overt rectal bleeding or taking fecal occult blood tests included 38 with early colorectal carcinoma treated surgically or endoscopically and 42 with colorectal adenoma excised endoscopically. Of 38 patients with early carcinoma, 22 presented overt rectal bleeding, in 14 the test was positive and in 2 it was negative. Thus, overt and/or occult bleeding was noted in 95% of 38 patients. Of 42 patients with adenoma, 16 presented overt bleeding, in 20 the test was positive and in 6 it was negative. Thus, overt and/or occult bleeding was noted in 86% of patients with adenoma excised endoscopically. The incidence of overt bleeding increased with the size of early carcinomas but was poorly correlated with the size of adenomas. With regard to the location of early carcinoma, overt bleeding was extremely common in rectal tumors and was seen in approx half of the patients with sigmoid tumors. Adenomas in patients with negative fecal occult blood tests were located mainly proximal to the sigmoid colon. The sigmoid colon has a tendency to bleed easily when rubbed with feces passing through a narrow lumen. Regarding the shape, overt rectal bleeding was more commonly seen in pedunculated adenoma and sessile early carcinoma. All 18 patients with carcinomas with submucosal involvement (sm carcinoma) had either overt or occult bleeding. Only 2 of 20 patients with intramucosal carcinoma (m carcinoma) had negative fecal occult blood tests. Carcinoma without an adenomatous component was similar to sm carcinoma in the pattern of bleeding. In contrast, carcinoma in adenoma was similar to adenoma in this respect. In adenoma, no significant correlation was noted between bleeding and severity of histological atypism. (17 Refs) (In JPN)

15. PREOPERATIVE VALUE OF PERIPHERAL BLOOD LYMPHOCYTES IN COLORECTAL CANCER.

Devesa Mugica JM, Morales Castineiras V, Custardoy Motilva A, Enriquez Valens P, Avila C
Centro Ramon y Cajal, Crtra. de Colmenar, km. 9,100, Madrid, Spain
Rev Esp Enferm Apar Dig; 60(1):47-50 1981

The purpose of this study was the evaluation of the relationship between peripheral blood lymphocytes (PBL) and the stage of disease, location, carcinoembryonic antigen (CEA), short term prognosis in cases of local or disseminated disease. In the 18 mo period (1978-1979), 78 patients with colorectal adenocarcinoma had determinations of the PBL and CEA. The same was done with 42 control patients with benign diseases, excluding inflammations, allergies, autoimmune diseases, radiotherapy, corticotherapy or cytotoxic drugs. The values for urea and bilirubin were within normal limits. No statistically significant relationship was found with stage, location, CEA, but there was a clear cut relationship with the short term prognosis. The 4 mo to 2 yr survival time of patients with local or disseminated colorectal cancer improved when preoperatory PBL values were above 2,000 lymphocytes/ml. Of 19 death, 12 were due to sepsis. Lymphocytopenia is probably due to immunodeficient state. Authors suggest antibiotic and immuno prophylaxis for preoperative patients with lymphocytopenia in suspected advanced or disseminated neoplastic disease. (12 Refs) (In SPA)

16. A COMPARISON OF TUBE LEUKOCYTE ADHERENCE INHIBITION ASSAY AND STANDARD PHYSICAL METHODS FOR DIAGNOSING COLORECTAL CANCER.

Ayeni AO, Thomson DM, MacFarlane JK, Daly D
(c/o Thomson), Montreal General Hosp., 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada
Cancer; 48(8):1855-1862 1981

In vitro antitumor immunity, measured by means of a tube WBC adherence inhibition (LAI) assay, was able to demonstrate early colorectal cancer in cases yet undiagnosed. Testing 106 patients attending a colonoscopy clinic, we found that 9 of 15 (60%) patients with colorectal cancer were LAI-positive. The nine included: five of six with Dukes' A and B; one of the two with Dukes' C; and three of seven with Dukes' D lesions. Of 58 patients without colon neoplasia, 1 had a positive test. By contrast, barium enema results were diagnostic for 13 of 15 (87%) cases and colonoscopy for 11 of 15 (73%). There were 32 colon polyps discovered by means of barium enema and colonoscopy. Of 13 adenomas removed, 4 had stimulated positive LAI responses. Of another 19 polyps not removed 2 incited positive LAI responses. Two patients with histor ies of recurrent adenomas were LAI-positive, though only one had a new polyp that could be detected by means of barium enema. For a procedure to be of diagnostic value for a given disease, sensitivity and specificity must be at least 1.0. If this sum is 2.0, the test is ideal. The sum of sensitivity and specificity for the tube LAI assay, barium enema, and colonoscopy were 1.58, 1.87, and 1.73, respectively, for colorectal cancer; 1.81, 2.0, and 2.0, respectively, for early colorectal cancer; and 1.42, 1.77, and 1.55 respectively, for advanced colorectal cancer. In this limited series of patients, the barium enema seems to be superior to the tube LAI assay for diagnosing colorectal cancer, but the difference in sensitivity and specificity is not statistically valid by the paired chi square test. The results of this study show conclusively, that the tube LAI is of diagnostic value and suggest its use for evaluating suspected cases, especially early ones, of colorectal cancer. (Author abstract) (33 Refs)

17. EVALUATION OF THE LEUCOCYTE ADHERENCE INHIBITION ASSAY IN THE DIAGNOSIS OF COLORECTAL CARCINOMA.

Leveson SH, Woodhouse LF, Giles GR
Univ. Dept. Surgery, St. James's Univ. Hosp., Leeds LS9 7TF, England
Clin Oncol; 7(3):183-191 1981

A prospective trial has been established in order to assess the accuracy of the leukocyte adherence inhibition (LAI) assay in diagnosing colorectal carcinoma. Estimates were performed on 26 patients with colorectal cancer, 22 patients with cancer of non-colorectal origin and 22 patients with benign disease. The results suggest that the assay is very accurate and specific in early cancer, but that the results become less reliable with increasing tumor burden. Practical problems associated with antigen preparation and storage are discussed. (Author abstract) (16 Refs)

18. EVALUATION OF POSSIBLE CAUSES OF DELAYED HYPERSENSITIVITY IMPAIRMENT IN CANCER PATIENTS.

Dominioni L, Dionigi R, Dionigi P, Nazari S, Fossati GS, Prati U, Tibaldeschi C, Pavesi F
Istituto de Patologia Chirurgica, Universita de Pavia, 27100 Pavia, Italy
JPEN; 5(4):300-306 1981

The role of tumor growth, malnutrition, and aging as etiologic factors of depressed delayed hypersensitivity response (DHR) was studied in patients (48 men, 63 women; 20-80 yr old) with solid tumors (20 stomach, 16 colon, 18 rectum, 27 breast, and 30 other cancers). The sex distribution, mean age, and mean serum albumin (SA) levels of the cancer patients and 56 controls (27 men, 29 women; 30-88 yr old) were not significantly different. The controls consisted of nonneoplastic patients, many of whom presented with clinical signs of overt malnutrition, who had been referred to the institute because of their poor general condition and high surgical risk. The mean SA levels of both these cancer patients and controls wer e significantly lower than the mean serum albumin level of well-nourished, age-matched controls. Significantly depressed values of SA and DHR were recorded in patients with stomach, colon, and rectum cancers. The stage of the tumor was inversely correlated with the SA level. Cancer patients presented a mean DHR that was not significantly different from the DHR of matched controls; however, the DHR of both groups were significantly lower than that of hospitalized patients, less than 50 yr old with minimal nonneoplastic diseases. All anergic cancer patients, except one, had tumors of the gastrointestinal tract and a very low mean SA level. The mean tumor stage of anergic cancer patients was significantly more advanced than in the remaining anergic cancer patients. Regression analysis indicated a significant correlation between the DHR and SA indicating that solid tumors cause malnutrition and that, subsequently, malnutrition causes depression of DHR. (57 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

19. ANTERIOR VERSUS ABDOMINOPERINEAL RESECTION FOR CARCINOMA OF THE RECTUM: A LITERATURE REVIEW.

Cohen LI
Dept. Medicine, Montefiore Hosp., Bronx, NY, 10467
Mt Sinai J Med (NY); 48(5):469-473 1981

Pathologic and anatomic studies indicated that anterior resection (AR) should equal abdominoperineal resection (APR) as a curative procedure for rectal carcinomas 8-13 cm above the dentate line. The studies implied that AR would be as effective in excising the gross lesion and in extirpating nodal metastases. A review of relevant comparative studies showed that AR was associated with a slightly higher 5-yr survival rate and slightly lower operative mortality and morbidity than APR. The 5-yr survivals in one study were 57% for AR (89 patients) and 46% for APR (93 patients). In another study, the 5-yr survival was 56% after AR (247 patients) and 47% after APR (277 patients). Local recurrence rates, however, were nearly identical with the two procedures; moreover, no superiority could be claimed for either when the 5-yr survival was compared for men and women. The decision to perform AR or APR should be predicated essentially on the distance of the lower tumor border from the anus. (22 Refs)

20. PREDICTION OF LOCAL RECURRENCES AFTER SURGERY FOR CARCINOMA OF THE MIDDLE RECTUM.

Hermanek P, Gunselmann W, Altendorf A, Gall FP, Horbach L
Abteilung fur Klinische Pathologie, Universitat Erlangen-Nurnberg, Erlangen, W. Germany
Langenbecks Arch Chir; 354(2):133-146 1981

A multivariate statistical method was developed for predicting the risk of local recurrence after curative surgery for carcinoma of the middle third of the rectum on the basis of completely and exactly documented follow-up data of 237 patients subjected to surgery during the period 1969-1978. Rectum extirpation was performed in 94 cases, resection with a wide safety margin (more than 30 mm) in 63, and resection with a narrow margin (11-30 mm) in 80. The incidence of local recurrences was 21/94 after extirpation, 10/63 after wide resection, and 31/80 after narrow resection. Forty of the 175 patients without local recurrence and 50/62 with local recurrence were dead at the time of reporting. The model to predict the risk of local recurrence was developed on the basis of seven variables: preoperatively determined distance of the tumor from the anocutaneous line (greater or smaller than 10 cm), tumor form (insular or circular), growth type (exophytic, endophytic, or ulcerated), largest tumor diameter (less than 30 mm, 31-50 mm, greater than 51 mm), in-depth infiltration (maximally the muscular layer or the subserous layer and deeper), number of involved lymph nodes (1-3 or greater than or equal to 4), and involvement of distant lymph nodes (yes or no). Using this model, the risk of local recurrence is calculated after anterior resection according to macroscopic findings on the specimen and to frozen section histology. If the risk calculated for anterior resection and extirpation are approx equal, the resection is ended by anastomosis; otherwise the operation will be extended to rectal extirpation. (14 Refs) (In GER)

21. RECURRENCE OF CARCINOMA OF THE COLON AND RECTUM AT THE ANASTOMOTIC SUTURE LINE.

Pihl E, Hughes ES, McDermott FT, Price AB
Dept. Surgery, Monash Univ., Melbourne, Australia
Surg Gynecol Obstet; 153(4):495-496 1981

A total of 1,315 patients were treated by potentially curative resection for a single primary malignant tumor of the large intestine. Thirty-five or 2.7% of the patients subsequently presented with a recurrent tumor at the site of the anastomosis. Fourteen of these patients were treated by further operation with curative intention, resulting in a median cancer-specific survival time of 41 mo. The prognosis after resection of a recurrence of the tumor at the suture line was significantly better, p = 0.001, than for patients in whom no further resection of palliative operation only was performed. None of the latter has survived for more than 30 mo after confirmation of the recurrence, with a median survival time of 8.5 mo. (Author abstract) (8 Refs)

22. PRESERVATION OF SPHINCTERS IN RECTAL CANCER RESECTION.

Bonardi O
No affiliation given
Minerva Chir; 36(12):873-876 1981

Rectal anatomy is presented in detail and different surgical techniques are discussed. Automatic circular sewing has increased the rate of anterior resection of deeper lesions. According to Duke's classification, Stage A growth is confined to the rectal wall (mucosa, submucosa, and muscular layer), Stage B growth has penetrated the wall and infiltrated serosa and perirectal tissue, and in Stage C metastases of the lymph nodes are present. Stage A disease may be cured when treated, Stage B has a 10 yr survival rate of 70%, and Stage C has 10 yr survival of 30%. Clinically, Stage A may be identified by diameter less than 4 cm, mobile lesion, no lymph nodes palpable on the posterior wall during rectal examination, and histologic examination showing well-differentiated cancer. St. Mark's Hospital in London recommends full thickness biopsy for identification of depth of invasion, even for the more superficial lesions. If 100 patients are selected according to such clinical criteria, only 10% would be identified Stage C, rather than the 50% expected for 100 unselected cases. If 100 selected patients had local resection, only 10% would receive inadequate treatment; when rectal resection is performed on 100 unselected patients mortality occurs in 13% of patients. Full thickness local resection is recommended; stenosis need not be feared due to adequacy of rectal ampulla. (5 Refs) (In ITA)

23. URETERAL INJURIES IN COLONIC SURGERY.

Cass AS, Bubrick MP
Dept. Surgery, Hennepin County Medical Center, Minneapolis, MN
Urology; 18(4):359-364 1981

Ureteral injury during colonic surgery has an incidence of 0.3 to 6%. The site of injury occurs at the level of ligature of the inferior mesenteric vessels during mobilization of the sigmoid, during division of the lateral rectal ligaments, and during reperitonealization of the pelvis. Techniques of prophylaxis, intraoperative diagnosis, and postoperative diagnosis are described. The main controversy in management between immediate definitive repair versus initial urinary diversion with delayed repair is discussed. (Author abstract) (40 Refs)

24. PREVENTION OF WOUND INFECTION IN ELECTIVE COLORECTAL RESECTIONS BY PREOPERATIVE CEPHAZOLIN WITH AND WITHOUT METRONIDAZOLE.

McDermott FT, Polglase AL, Johnson WR, Hughes ES

Dept. Surgery, Monash Univ., Alfred Hosp., Prahran, Victoria 3181, Australia

Aust NZ J Surg; 51(4):351-353 1981

Fifty patients were admitted to a prospective controlled double blind trial for assessment of the effect of preoperative im cephazolin with oral metronidazole or placebo on the incidence of wound infection in patients requiring treatment by elective large intestinal resection. All patients were operated upon by one surgeon. After exclusion of two patients who died postoperatively 48 were analyzed. No wound infection occurred in 22 patients receiving cephazolin with metronidazole. One (3.8%) infection developed in 26 patients receiving cephazolin with placebo. The difference did not attain statistical significance. Preoperative im cephazolin with or without metronidazole provides an effective and safe method of chemoprophylaxis for elective colorectal resection. (Author abstract) (8 Refs)

25. TINIDAZOLE AS PREVENTIVE TREATMENT IN ELECTIVE COLONIC SURGERY.

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Scand J Infect Dis; 13(2):137-140 1981

In a double-blind study in patients subjected to elective bowel surgery, the effects of tinidazole (TDZ), an analogue of metronidazole, on postoperative infections was compared to that of placebo. The TDZ group was comprised of 14 males and 19 females, aged 18-88 yr; the placebo group 21 males and 10 females, aged 30-88. All patients underwent mechanical bowel preparation for 2 days. Patients received either 1 g TDZ or placebo at 12 noon the day before operation and again 4-7 hr before surgery. Two of the 27 TDZ patients developed wound sepsis, 2 perineal wound sepsis and 4 a complicating pneumonia in the postoperative period. In the placebo group 12 developed wound sepsis, 7 intraabdominal septic complications, 4 perineal wound sepsis, 3 urinary tract infections and 2 pneumonia. Antibiotic treatment for these infections was given to 13 in the placebo group and 6 in the TDZ group. Total antibiotic usage was 465 daily doses (36/patient) in the placebo group compared to 49 (8/patient) in the TDZ group. In the TDZ group wound cultures showed growth only of facultative organisms while in the placebo group both facultative and anaerobic organisms developed. No side effects due to TDZ were observed. TDZ can be recommended for preventive 1-day treatment before bowel surgery. (21 Refs)

26. MANAGEMENT OF CARCINOMA OF ANAL CANAL.

Schneider TC, Schulte WJ

Dept. Surgery, Wood Veterans Admin. Medical Center, Medical Coll. Wisconsin, Milwaukee, WI, 53193

Surgery; 90(4):729-734 1981

The application of various treatment modalities in the management of carcinoma of the anal canal remains controversial. Forty-nine patients were reviewed from the affiliated hospitals of the Medical College of Wisconsin. Exclusions for postoperative deaths, associated vulvar carcinoma, and lack of follow-up left 35 patients for determinate study. The overall 5-yr survival rate was 28.6% (10 of 35). When reviewed by stage of disease, a direct relationship between advanced stage and decreased survival (ie, 60% 5-yr survival rate with Stage I, 25% with Stage II, and 14.3% with Stage III) was noted. Further reclassification of Stage III, nodal involvement, showed the same survival for perirectal nodal involvement as for synchronous inguinal node involvement. Seven of 10 5-yr survivors received a combined surgery-radiotherapy approach. In addition, in those patients receiving tumoricidal radiation pre- or postoperatively, no local recurrence was demonstrated. A treatment protocol of abdominal perineal resection, with combined radiation therapy for locally advanced lesions, is proposed. (Author abstract) (24 Refs)

27. INTERSTITIAL CURIETHERAPY IN THE TREATMENT OF ANORECTAL CARCINOMA.

Jackson BR

Dept. Surgery, Southern California Cancer Center, Los Angeles, CA

Modern Interstitial and Intracavitary Radiation Management. George FW, ed. New York, Masson Publishing USA, Inc., Cancer Management, Vol. 6, 132 pp., 1981.

Results of interstitial curietherapy and external irradiation treatment for anorectal neoplasms are reported. Patients consisted of a select group demonstrating one or more of the following: poor surgical risk, extensive primary or recurrent tumor, distant incurable metastasis, and refusal of surgery. Of 31 cases, 3 had primary rectal adenocarcinoma (PRA), 20 had recurrent rectal adenocarcinoma (RRA), and 8 had primary or recurrent anal canal carcinoma (ACC). Twenty-five patients were treated with a combination of external radiation and 192Ir implants utilizing a perineal template and afterloading technique (described in detail); four recurrent rectal adenocarcinoma patients also received permanent seed implants of 125I at laparotomy. One of three PRA patients (av age 84 yr) is alive with tumor; the remaining two died of unrelated causes. Of 20 RRA patients (av age 72 yr), 12 are alive, 7 with tumor and 5 with no evidence of disease; 8 have died, 5 due to tumor. In ACC cases (av age 65 yr), 5/8 have survived, 3 with tumor and 2 with no evidence of disease; 2/3 who died had tumor metastases. Complications included diarrhea with incontinence and stenosis or stricture (the most severe and appearing with approx equal distribution in the three groups), necrosis ranging from moderate to severe, rectovaginal fistula, and milder symptoms such as pain, induration, mucositis, and bleeding. The treatment method is thought to offer significant local control and effective palliation with an acceptable rate of complications in this select group of patients. (15 Refs)

28. HYPERTHERMIA IN ENDORADIOTHERAPY.

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Dept. Radiology, Radiation Oncology Div., Arizona Health Sciences Center, Tucson, AZ

Modern Interstitial and Intracavitary Radiation Management. George FW, ed. New York, Masson Publishing USA, Inc., Cancer Management, Vol. 6, 132 pp., 1981.

The use of localized hyperthermia along with low dose-rate radiation including interstitial and intracavitary sources is discussed; results of treatment in eight cases are reported. The combination of hyperthermia with endocurietherapy is justified for the following reasons: (1) hyperthermia is capable of killing both oxygenated and hypoxic tumor cells, (2) cells in the S phase are sensitive to hyperthermia but are often resistant to radiation, (3) hyperthermia inhibits repair of sublethal radiation damage, and (4) hyperthermic enhancement of radiation cytotoxicity is greatest at low dose rates. Patient dia gnoses were breast carcinoma, undifferentiated carcinoma of parotid skin nodules, carcinoma of gallbladder with metastases, unresectable rectal carcinoma, recurrent carcinoma of mobile tongue, melanoma of vulva, rectal carcinoma with perineal recurrence, and carcinoma of tongue. Tumors were heated resistively with radiofrequency current between 500 kilohertz and 3 megahertz, using Ra or 192Ir needles as heating electrodes. Dose varied, but the aim was to give 4000 rad in 4 days plus 43 C for 30 min. Between 80 and 100% or 'acute' regression was seen in 6/8 patients. Complications which occurred in two responding patients were a superficial burn of the buttock and skin necrosis. The necrosis developed after a max dose of 5000 rad plus 43 C for 45 min; 4000 rad plus 43 C for 30 min may represent the limits of tolerance. The relative contribution of hyperthermia to tumor response was difficult to assess, but rapid tumor regression within a few min of heating was observed in the two patients with tumors of the tongue. (4 Refs)

29. CHEMOTHERAPY FOR COLORECTAL CANCER WITH A COMBINATION OF PALA AND 5-FU.

Bedikian AY, Stroehlein JR, Karlin DA, Bennetts RW, Bodey GP, Valdivieso M

Dept. Developmental Therapeutics, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030

Cancer Treat Rep; 65(9):747-753 1981

Fifty-one previously untreated patients with advanced, measurable colorectal cancer were randomized to receive single doses of phosphonacetyl-L-aspartate (PALA) and 5-fluorouracil (5-FU) either weekly (24 patients) or daily for 5 days every 4 wk (27 patients). In both schedules the daily dose of PALA was administered iv over 1 hr, while the dose of 5-FU was administered iv over 30 min, starting 3 hr after completion of the PALA dose. Doses of both drugs were changed simultaneously, based on toxic effects. Partial responses were seen in 4 of 24 evaluable patients receiving the weekly regimen and in 3 of 26 patients receiving the 5-day regimen. Skin rash, mucositis, and diarrhea were the dose-limiting toxic effects in both treatment regimens. These toxic effects were more common and severe at higher doses and on the weekly schedule. Myelosuppression was mild to moderate, even at the highest dose schedules. The combination of PALA and 5-FU at the doses and schedules used in this study did not significantly increase the activity of 5-FU. Further evaluation of these doses and schedules for activity against colorectal cancer is not warranted. (Author abstract) (20 Refs)

30. MELPHALAN, VINCRISTINE, AND 5-FU IN ADVANCED COLONIC CARCINOMA: RESULTS OF A PILOT STUDY.

Ashenhurst J, Bitran JD, Robin E, Desser RK, Shapiro C, Kozloff MF, Billings AA
(c/o Bitran) Div. Hematology/Oncology, Dept. Medicine, Michael Reese Hosp. and Medical Center, 29th St. and Ellis Ave., Chicago, IL, 60616
Cancer Treat Rep; 65(9):869-872 1981

The results of treatment with melphalan, vincristine, and 5-fluorouracil (MFV) in 32 patients with advanced colonic carcinoma are reported. The objective response rate among 31 patients with measurable disease was 16% (5 patients responded). The projected survival for all 32 patients was 277 days. Patients with objective response to MVF had a projected survival of 314 days, significantly longer than the survival of patients with no response to therapy, 84 days (p = 0.01). While toxic effects were mild with MVF, this regimen appears to have no greater activity in advanced colonic carcinoma than therapy with 5-FU alone or in combinations with nitrosoureas. (Author abstract) (16 Refs)

31. PHASE II TRIAL OF IV 6-THIOGUANINE IN ADVANCED COLORECTAL CARCINOMA.

Britell JC, Moertel CG, Kvols LK, O'Connell MJ, Rubin J, Schutt AJ
(c/o Rubin) Medical Oncology and Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, MN, 55901
Cancer Treat Rep; 65(9):909-910 1981

Oral 6-thioguanine (6-TG) is an S-phase antimetabolite with significant activity against acute leukemia. Preliminary reports of activity of iv 6-TG indicated significant activity against advanced colorectal cancer. We conducted a Phase II study of iv 6-TG in 29 patients with advanced measurable colorectal cancer. Only one transient partial response occurred. Toxic effects included mild myelosuppression, nausea, vomiting, and minor ECG changes. We discourage further use of iv 6-TG in the dose and schedule we used to treat advanced colorectal cancer. (Author abstract) (4 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

32. COLORECTAL CARCINOMA IN PATIENTS UNDER 35 YEARS OF AGE.

Klempa I, Menzel J, Rheinheimer R
Zentrum der Chirurgie, Abteilung fur Allgemein- und Abdominalchirurgie, Johann-Wolfgang-Goethe-Universitat, Th.-Stern-Kai 7, D-6000 Frankfurt/M, W. Germany
Zentralbl Chir; 106(15):1033-1041 1981

The incidence of colorectal carcinoma in young people is increasing. The histories of 569 patients had been worked up. Twenty nine of our patients were under 35 yr of age. The main symptoms are the same in both groups. The severeness of the disease - as expressed in TNM-staging is comparable. We point out, that the incidence of mucoid carcinoma is 3x higher in young people. Nevertheless, prognosis is only dependent on the phase at the time of discovering the tumor. Concerning prognosis there is no difference between the two age groups. (Author abstract) (19 Refs) (In GER)

33. THE PROGNOSTIC IMPLICATIONS OF OBSTRUCTING LEFT COLONIC CANCERS.

Schein CJ, Gemming RH
(c/o Gemming), Montefiore Hosp. Medical Center, 111 East 210 Street, Bronx, NY, 10467
Dis Colon Rectum; 24(6):454-455 1981

Obstructing colonic cancers pose a difficult problem from the points of pathology and prognosis. There are many reports in the literature pertaining to the management and treatment of patients with left-sided colonic obstruction. This study documents the more advanced state of cancers with acute obstruction. (Author abstract) (12 Refs)

34. PROLONGED SURVIVAL AS A COMPONENT OF HEREDITARY BREAST AND NONPOLYPOSIS COLON CANCER.

Lynch HT, Albano W, Recerbaren J, Lynch PM, Lynch JF, Elston R
Creighton Univ., 2500 California St., Omaha, NE, 68178
Med Hypotheses; 7(9):1201-1209 1981

The survival in hereditary breast and colorectal cancers are compared with corresponding population norms. These findings form the basis for discussion of an hypothesis with mechanisms of host control. Survival was tabulated retrospectively for 106 patients with hereditary breast cancer (20 unrelated families) and 117 patients with hereditary carcinoma of the colon (18 unrelated families, none exhibiting multiple polyposis of the colon). Comparison data were obtained from the long-term audits of the American College of Surgeons (ACS) Tumor Registry for Breast and Colon Cancer. No appreciable differences in presenting stage were observed between the hereditary patients and those of the ACS Registry. The av age of diagnosis of the 106 hereditary breast cancer patients was 49, with 35.2% under age 45. The av age at diagnosis in the ACS Breast Tumor Registry Study was 57 yr with only 15.9% of the patients diagnosed under age 45. Of 106 breast cancer patients, 85 were followed for at least 5 yr with 57/85 remaining disease-free. Of the 73 patients surviving 10 yr or more, 39 were disease-free. The 5-yr disease-free survival in the ACS group was only 45.2%. The mean age at diagnosis of the 117 patients with hereditary nonpolyposis colon cancer was 46 yr, with 36.5% less than 40 yr old at the time of diagnosis. Only 6% of the patients with colon cancer in the ACS Registry were under age 40. The overall 5-yr disease-free survivorship was 52% in the hereditary colon cancer population, significantly better than the 35.3% rate in the ACS population. Improved survival in this limited number hereditary breast and colon cancer patients suggested that host factors may play a major role in not only etiology, but natural history of cancer as well. Clinical observation and cancer survival, spontaneous regression of cancer and cancer resistance, and an hypothesis of survival benefit and implications of this hypothesis for therapeutic trials are discussed. (28 Refs)

35. MICROANGIOPATHIC HEMOLYTIC ANEMIA, THROMBOCYTOPENIA, AND RENAL FAILURE IN PATIENTS TREATED FOR ADENOCARCINOMA.

Kressel BR, Ryan KP, Duong AT, Berenberg J, Schein PS
(c/o Schein) Div. Medical Oncology, V. T. Lombardi Cancer Res. Center, Georgetow n Univ. Medical Center, Washington, DC, 20007
Cancer; 48(8):1738-1745 1981

Microangiopathic hemolytic anemia and thrombocytopenia secondary to disseminated intravascular coagulation is a well-described complication of widely metastatic carcinoma. The authors report four cases of gastric carcinoma, one case of colon cancer, and one case of adenocarcinoma of unknown primary in which the patient developed a syndrome analogous to thrombotic thrombocytopenic purpura, consisting of microangiopathic hemolytic anemia, thrombocytopenia, and renal failure without definite evidence of disseminated intravascular coagulation. In contrast to previous reports, postmortem examination in three of the cases revealed no recurrence or only microscopic foci of residual tumor. In the remaining three, there was clinical and pathologic evidence of grossly disseminated carcinoma. Also in contrast to previous cases, all patients evidenced azotemia and proteinuria at the onset of the syndrome and ultimately uremia was a contributing cause of death. Coagulation profiles showed prolonged thrombin times and elevated fibrin degradation products in four instances and did not distinguish the patients with grossly metastatic disease from those with no tumor or only microscopic residua. Circulating immune complexes containing carcinoembryonic antigen were found in the patient with metastatic colon carcinoma. The syndrome was clinically identical whether or not grossly metastatic tumor was present, and it should not be attributed to advanced disease without definite clinical or pathologic evidence of a recurrence. (Author abstract) (34 Refs)

36. EXPERIMENTAL RADIOIMMUNOTHERAPY OF A XENOGRAFTED HUMAN COLONIC TUMOR (GW-39) PRODUCING CARCINOEMBRYONIC ANTIGEN.

Goldenberg DM, Gaffar SA, Bennett SJ, Beach JL
Div. Experimental Pathology, MS-409, Univ. Kentucky Coll. Medicine, Lexington, KY, 40536
Cancer Res; 41(11,part1):4354-4360 1981

Experiments were undertaken to evaluate the antitumor effects of 135I-labeled goat antibody Ig G prepared against carcinoembryonic antigen in hamsters bearing the carcinoembryonic antigen-producing GW-39 human colonic carcinoma. At a single injection of 1 mCi 131I and higher, a marked growth inhibition of GW-39 tumors, as well as a considerable increase in the survival time of the tumor-bearing hamsters, could be achieved. At a dose of 1 mCi, the radioactive affinity-purified antibody appeared to be superior to radioactive normal goat Ig G in influencing tumor growth and survival time, but no significant difference could be seen at the higher dose of 2 mCi given. Radiobiological calculations indicated that the tumors received, at up to 20 days after therapy, 1,325 rads for the specific antibody and only 411 rads for the normal Ig G preparation. These findings encourage the further evaluation of anti bodies to tumor markers for isotopic cancer therapy. (Author abstract) (36 Refs)

37. INHIBITION OF THE PLATELET-AGGREGATING ACTIVITY OF TWO HUMAN ADENOCARCINOMAS OF THE COLON AND AN ANAPLASTIC MURINE TUMOR WITH A SPECIFIC THROMBIN INHIBITOR, DANSYLARGININE N-(3-ETHYL-1,5-PENTANEDIYL)AMIDE.

Pearlstein E, Ambrogio C, Gasic G, Karpatkin S
(c/o Karpatkin) Dept. Medicine, New York Univ. Medical Sch., New York, NY, 10016
Cancer Res; 41(11,part1):4535-4539 1981

Platelets are required for certain experimental metastases. Several lines of animal tumor cells aggregate platelets in vitro and in vivo. Previous studies with one of these lines, an SV40-transformed 3T3 mouse fibroblast (SV3T3) have revealed that the platelet-aggregating material is an extractable membrane-associated sialolipoprotein which requires divalent cation, complement, and a heat-stable plasma component for activity. Little information is available on the interaction of human tumors with platelets. We now report on the ability of two human adenocarcinomas of the colon (LoVo and HCT-8) and an anaplastic mouse tumor (Hut-20) to aggregate platelets by a different mechanism, the generation of thrombin. These spontaneous cell lines aggregate human or rabbit platelet-rich plasma after a 1-to 2-min lag period. This is often followed by a visible clot. Unlike SV3T3 cells, aggregation by LoVo, HCT-8, and Hut-20 cells is not inhibited by neuraminidase, trypsin, or cobra venom factor. These three cell lines markedly shorten the recalcification time of citrated plasma, whereas SV3T3 cells do not. Phospholipase A2 treatment inhibits the shortening of the recalcification time for the three tumors; this parallels its inhibitory effect on platelet aggregation. LoVo, HCT-8, and Hut-20 cells generate thrombin via the 'tissue factor' coagulation pathway (using coagulation factor-deficient substrates). Dansylarginine-N-(3-ethyl-1,5-pentanediyl)amide, a highly specific, potent antithrombin antagonist, inhibits LoVo-, HCT-8-, and Hut-20-induced platelet aggregation at 4 to 15 uM, whereas its effect on SV3T3 cells is negligible. If platelets are required for certain human tumor metastases, dansylarginine-N-(3-ethyl-1,5-pentanediyl)amide, or other antithrombin agents, may prove to be valuable therapeutic agents. (Author abstract) (37 Refs)

38. ADENOSINE AND GUANOSINE 3',5' CYCLIC MONOPHOSPHATE PHOSPHODIESTERASE ACTIVITIES IN RAT SMALL AND LARGE BOWEL FOLLOWING SINGLE AND MULTIPLE EXPOSURES TO 1,2-DIMETHYLHYDRAZINE.

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Drug Chem Toxicol; 4(2):161-172 1981

The affect of the colon carcinogen, dimethylhydrazine (DMH: 20 mg/kg, sc) on the hydrolytic activities of cyclic AMP (cAMP) and guanosine 3',5'-cyclic monophosphate (cGMP) phosphodiester ases (PDE) in the small and large intestines of adult male outbred rats was determined. Following injection of DMH, an almost immediate increase in cAMP-PDE activities in the colon tissue was observed. These elevated activites, which had increased after 1 day to greater than three times that in untreated colon, returned to normal value after approx 5 days after exposure. In contrast, the cGMP-PDE activities seemed only slightly changed by the exposure to DMH. Chronic exposures at weekly intervals to the DMH had little effect on PDE activites during the early phases of tumor activity. However, at the end of wk 20, exposed colon tissues had elevated cAMP-PDE levels similar to those in cancer cells. Approx 10-15% of DMH-treated rats developed small bowel cancer. A single exposure to DMH produced a significant increase in both the cAMP- and cGMP-PDE activities. Chronic exposure to DMH resulted in little apparent PDE changes in the small intestine until approx wk 20 at which time cAMP-PDE levels were similar to those measured in small bowel tumor cells. Ratios of cAMP and cGMP and cAMP-PDE and cGMP-PDE measured in the colon tissue following single and double DMH exposure were plotted against time. The measurements suggested that cyclic nucleotide content may be a reflection of tissue insult by an environmental toxicant. (19 Refs)

39. BIOCHEMICAL AND CLINICAL EFFECTS OF SELENIUM ON DIMETHYLHYDRAZINE-INDUCED COLON CANCER IN RATS.

Jacobs MM, Forst CF, Beams FA
Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NE, 68105
Cancer Res; 41(11,part1):4458-4465 1981

The biochemical and clinical effects of selenium (Na2SeO3) on 1,2-dimethylhydrazine (DMH)-induced colon carcinogenesis in male Sprague-Dawley rats are presented. A 4-ppm selenium supplement to the drinking water was provided before, during, and after 20 weekly injections of 20 mg DMH per kg body wt. Immediately after the 20th DMH injection, part of the rats were sacrificed. The incidences of colon tumors in groups provided selenium before DMH, before and during DMH, and only during DMH treatment were reduced to 39, 43, and 36%, respectively. The incidence in the DMH only control was 63%. Other rats in all treated and control groups were maintained up to 5 mo post-DMH treatment. At 10-wk intervals throughout the study, selected blood and tissue components were analyzed. The following hematological changes correlated with DMH treatment. (a) Serum glutamic oxalacetic transaminase increased 2-fold (normal, 66 +-14 g/dl). (b) Serum alkaline phosphatase increased 24% (normal, 166 +-56 units/liter). (c) Serum protein decreased 14% (normal, 6.77 +-0.48 g/dl). (d) White blood count increased 2-to 3-fold (normal, 7.7 +-2.7 x 10(3)/cu mm). And (e) Hb decreased 67% (normal, 18.1 +-1.3 g/dl). The magnitude of these changes varies with each selenium treat ment group and with each 10-wk analysis period. Provision of 4 ppm selenium doubled both liver and blood selenium levels compared to supplemented controls. The effects of selenium and DMH treatments on glutathione peroxidase and beta-glucuronidase activities and on sialic acid are presented. Possible mechanisms by which selenium protect against DMH-induced neoplasia are discussed. (Author abstract) (40 Refs)

40. UTILIZATION OF BLOOD ANALYSES TO EVALUATE METABOLIC CHANGES IN CONTROL AND 1,2-DIMETHYLHYDRAZINE-TREATED ADULT MALE FISCHER RATS.

Southern JT, Schiller CM
(c/o Schiller) Lab. Organ Function and Toxicology, Natl. Inst. Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC, 27709
Cancer Lett; 14(1):47-54 1981

Seven-wk-old male Fischer rats received 1,2-dimethylhydrazine hydrochloride (DMH: 35 mg/kg) by intubation and were examined 1.5 yr later for tumor incidence at which time blood analyses were performed. The incidence of tumors in the treated animals was 78%, while no tumors were seen in controls. Most of the tumors were in the colon. There were statistically significant differences between treated and control animals in total WBC, percentage of lymphocytes, and in the percentage of eosinophils and segmented cells. Treated animals had a lower lymphocyte number and an elevated level of polymorphonuclear WBC. Treated animals had decreases in serum Na and K and increase in phosphate; the ion balance of treated animals was decreased. Serum albumin levels were significantly elevated, total protein levels were lower, SGOT and SGPT levels were decreased and creatine phosphokinase level was elevated in treated animals. The albumin/globulin ratio was increased 3.5-fold in the treated animals. Creatinine concentration was decreased in the treated animals. These data obtained using routine hematoplasia analysis and biochemical analysis with the Sequential Multiple Analyzer Computer Multitest system indicate that the routine clinical analyses as performed with these techniques can be readily adapted to evaluate samples from laboratory animals. (29 Refs)

41. COMPARISON OF THE CARCINOGENICITY OF METHYLAZOXYMETHANOL-BETA-D-GLUCOSIDURONIC ACID IN CONVENTIONAL AND GERMFREE SPRAGUE-DAWLEY RATS.

Laqueur GL, Matsumoto H, Yamamoto RS
(c/o Matsumoto) Dept. Agricultural Biochemistry, Univ. Hawaii, 1800 East-West Rd., Honolulu, HI, 96822
JNCI; 67(5):1053-1055 1981

Methylazoxymethanol-beta-D-glucosiduronic acid (MAM-GlcUA) was administered to young adult male Sprague-Dawley rats by oral and ip routes. Most neoplasms developed in rats that had received the compound po. The most prevalent site for the neoplasms was the intestinal tract, predominantly the colon. Comparatively fewer tumors occurred in the liver and kidneys. Germfree rats did not develop tumors when MAM-GlcUA was administered either po or ip. (Author abstract) (9 Refs)

42. URETEROSIGMOIDOSTOMY AND COLON CARCINOGENESIS.

Bristol JB
Univ. Dept. Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, England
Science; 214(4518):351 1981

A published hypothesis that anastomotic tumors in the rat are caused by urinary enzymes activating fecal procarcinogens is questioned. The authors suggest that the development of tumors at sites of intestinal anastomosis is more likely to result from hyperplasia provoked by surgical trauma or the pressure of the suture material. Until some of the etiologic uncertainties are resolved, it is premature to conclude that the use of colon conduits in children is entirely free from the risk of subsequent carcinoma. (8 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

43. CARCINOMA OF THE LARGE INTESTINE WITH SCHISTOSOMIASIS - ANALYSIS OF 279 CASES.

Zhao E, Weng Y
Dept. Surgery, Hangzhou Cancer Hosp., Hangzhou, People's Republic of China
Zhonghua Zhongliu Zazhi; 3(1):67-69 1981

Clinical findings are described for 279 cases of large intestinal carcinoma with schistosomiasis (males/females ratio 1.85/1; aged 20-69 yr) and compared to those of 653 cases without schistosomiasis (males/females ratio 1.6/1; aged 16-69 yr) seen between 1963 and 1977. Most of the carcinomas were located in the rectum and sigmoid colon. No significant difference was observed in the histopathological classification of the two groups. However, Dukes' staging and lymph node metastatic status revealed considerably less lymph node metastasis and earlier Dukes' stage in the complicated than in the non-complicated group. The 5-yr survival rates in both groups were the same (approx 53%) though the operative mortality in the complicated group was much higher (3.42% vs 0.80%). The resection rates of the complicated and non-complicated groups were 59.34% and 65.49% respectively. It is postulated that schistosomiasis may lead to the development of carcinoma in the large intestine. (3 Refs) (In CHI)

44. CANCER OF THE COLON AND SCHISTOSOMIASIS.

En-Sheng Z
Hangzhou Cancer Hosp., Hangzhou, Zhejiang Province, China
J R Soc Med; 74(9):645 1981

Colorectal cancer incidence rates are given for Zhejiang Province, China, where intestinal schistosomiasis is endemic. Studies conducted by the pathology departments of several hospitals confirmed the causal relationship between schistosomiasis and large intestine cancer. (9 Refs)

45. CHOLECYSTECTOMY AND COLON CANCER.

Svastits E, Ulyok Z, Besznyak I, Ihasz M
Sebeszeti Osztaly, Orszagos Onkologiai Intezet, Budapest, Hungary
Orv Hetil; 122(31):1889-1890 1981

The possible relationships between cholecystectomy and colorectal cancer were st udied Colorectal cancer was diagnosed in a series of 589 patients (283 women and 306 men) during a 10-yr period. The anamnestic data revealed cholecystectomy preceding the diagnosis of colorectal carcinoma by at least 2 yr in 25/589 patients (in 17/283 women and 8/306 men). Previous cholecystectomy was found in the anamnestic data of 12 patients in another series of 386 patients with colorectal cancer during a 10-yr period. The findings fail to suggest cholecystectomy to be a predisposing factor for colorectal cancer, as was indicated by data in the literature. (12 Refs) (In HUN)

46. COLORECTAL CANCER - TUBERCULOSIS CONNECTION.

Goulston E
Royal North Shore Hosp. Sydney, 135 Macquarie St., Sydney, New South Wales 2000, Australia
Med J Aust; 1(12):637-638 1981

Tuberculosis is common in countries with a low incidence of colorectal cancer. A survey was made to determine whether there was any difference in mortality from colorectal cancer in Australia between matched groups with, and without, tuberculous disease. Four hundred consecutively decreased tuberculous patients were compared with a similar number proved not be have contracted any tuberculous infection, and were matched by age, sex, yr of death, and socioeconomic ethnic status. There was a statistical significance (p less than 0.01) for colorectal and other gastrointestinal cancers, but not for other cancers. In the non-tuberculous group, there were 21 deaths from colorectal and 24 deaths from other gastrointestinal cancers compared to 7 deaths from colorectal and 7 from other gastrointestinal cancers in tuberculous patients. Increased immunity against the tubercle bacillus may have played a part in these findings. (Author abstract) (5 Refs)

47. CANCER AND DRINKING WATER IN LOUISIANA: COLON AND RECTUM.

Gottlieb MS, Carr JK, Morris DT

Dept. Medicine, Dept. Biostatistics and Epidemiology, Tulane Univ. Sch. Medicine, 1430 Tulane Ave., New Orleans, LA, 70112

Int J Epidemiol; 10(2):117-125 1981

A case-control mortality study conducted in 20 parishes (counties) of South Louisiana to determine what relationship drinking Mississippi River water might have on mortality from colon or rectal cancer, found a significant risk for rectal cancer associated with surface water. Rectal and colon cancer deaths (692 and 1,167) from 1969 to 1975 were matched to non-cancer deaths by age at death (+-5 yr), yr of death, sex and race, and within groups of parishes with similar industrial and urban-rural characteristics, each group being defined so as to ensure that it included as nearly as possible equal populations using water from ground and surface sources, based on the 1970 census. Colon cancer did not relate significantly to any water variable, but rectal cancer associated strongly with surface, or Mississippi River, water. The odds ratio for rectal cancer between those who were born and died on ground water was 2.07 with 95% CI: (1.49-2.88). A multi-dimensional emergency contingency table analysis found the association between rectal cancer and surface water significant at the 0.0001 level and not dependent on age, race sex or yr of death. The risk for men was slightly higher than for women, but both sexes showed an increased risk. Chlorination also associated significantly with rectal cancer. Among those who used river water, the risk increased inversely as the distance from the mouth, with greater risk downstream from the many industries which line the river. (Author abstract) (24 Refs)

48. CANCER OF THE COLON AND RECTUM IN THE COLOURED POPULATION OF JOHANNESBURG. RELATIONSHIP TO DIET AND BOWEL HABITS.

Maisto OE, Bremner CG

(c/o Bremner) Dept. Surgery, Univ. Witwatersrand Medical Sch., Esselen St., Hillbrow, Johannesburg, 2001, Republic of South Africa

S Afr Med J; 60(15):571-573 1981

In the Colored population of Johannesburg, the incidence of carcinoma of the colon and rectum estimated over an 11-yr period (1970-1980) is 133 and 108/100,000 respectively per yr. This is lower than the incidence reported in Whites and appears to be even lower than that reported in South African and Zimbawean Blacks. A survey of dietary factors in this population showed a diet which was high in protein, low in fats and high in bulk. The frequency of bowel action was higher than in both Whites and Blacks. These factors support Burkitt's hypothesis which states that races with a high-bulk diet have a lower incidence of large-bowel cancer. (Author abstract) (16 Refs)

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. SCREENING FOR COLORECTAL NEOPLASIA IN ASYMPTOMATIC PATIENTS USING FLEXIBLE FIBEROPTIC SIGMOIDOSCOPY.

Wherry DC
Dept. Surgery, Georgetown Univ., 916-19th St., NW, Suite 814, Washington, DC, 20006
Dis Colon Rectum; 24(7):521-522 1981

Four hundred seventeen asymptomatic patients with an av age of 52 yr underwent screening flexible fiberoptic sigmoidoscopy. Seventy-three polyps were detected in 52 patients with a 17.5% detection rate. Half were above 2.5 cm and one-third were greater than 1.0 cm in size. Biannual follow-up of these

HE 20. 3173/2:

patients is planned to determine the efficacy of this screening procedure combined with removal of all polyps in preventing the development of colorectal cancer. (Author abstract) (6 Refs)

2. NEW TECHNIQUE TO STAGE EARLY RECTAL CARCINOMA BY COMPUTED TOMOGRAPHY.

Hamlin DJ, Burgener FA, Sischy B
Dept. Radiology, Univ. Florida Coll. Medicine, Box J-374, JHMHC, Gainesville, FL, 32610
Radiology; 141(2):539-540 1981

A new technique incorporating rectal distension with air, an iv injection of glucagon (1 mg), and an iv infusion of diatrizoate (300 ml) is described as a method for staging early rectal carcinoma by computed tomography. (Author abstract) (5 Refs)

3. ROLE OF CEA RADIOIMMUNODETECTION IN THE MANAGEMENT OF COLORECTAL CANCER (MEETING ABSTRACT).

Goldenberg DM, Kim EE, Deland FH, Bennett SJ
Division of Experimental Pathology, University of Kentucky, Lexington, KY, 40536
Oncodev Biol Med; AbstractsBook,1:P62 1981

Radioactive antibodies to carcinoembryonic antigen (CEA) have been shown to detect and locate CEA-producing tumors in man by the method of radioimmunodetection. Although this method is still rapidly developing and improving, clinical advantages have been attained in a number of patients in whom tumor recurrence or metastasis was suspected. Over 52 patients with a history of confirmed colorectal cancer received an iv injection of between 1 and 2.5 mCi of 131-I-labeled, affinity-purified, goat antibody IgG against CEA, followed by total-body photoscanning. Blood-pool and non-target sites or radioactivity were reduced by subtracting the images derived by injection of 99m-technetium components from the 131-I scans. In 10 of the 52 patients, sites of occult cancer could be located and then confirmed by surgery or other methods when, prior to radioimmunodetection, standard detection measures failed to reveal these sites. Elevated CEA plasma levels did not hinder successful tumor detection. It is concluded that cancer radioimmunodetection with highly purified antibodies to CEA is a useful procedure for pre- and post-operative evaluation of patients with CEA-producing colorectal cancer, sometimes revealing sites of tumor not disclosed by other procedures. (no Refs)

4. PORTAL VEIN LIVER SCANNING FOR EARLY DETECTION OF LIVER METASTASES IN COLORECTAL CANCER (MEETING ABSTRACT).

Mooney B, Critchley M, Grime S, Taylor I
Departments of Surgery and Nuclear Medicine, Royal Liverpool Hospital, Liverpool, England
Gut; 22(5):A436 1981

The methods currently available for the preoperative detection of colorectal liver metastases are limited in their ability to detect small lesions. This has both prognostic and therapeutic implications. Access to the portal circulation via the obliterated umbilical vein is available and is used for the cytotoxic treatment of established liver metastases as well as delivery of adjuvant therapy. In this st udy the cannulated umbilical vein has been used to perform (1) portal venography; (2) liver blood flow measurements using Xenon 133 clearance; and (3) liver perfusion studies using Tc99m microspheres. A portal venogram and hepatogram phase are obtained. Liver blood flow and perfusion studies were performed using a gamma camera with online computer and data storage facilities. This allowed qualitative and quantitative measurements of blood flow to different areas of the normal and metastatic liver. The results of these studies have been compared with preoperative Tc99m sulphur colloid and ultrasound scans of the liver as well as liver function tests. The initial results of these studies suggest that as many as 30% of patients with macroscopically normal liver at initial surgery for colorectal cancer have evidence of metastatic disease. These techniques may allow prognosis to be refined and treatment to be planned on a more rational basis. (no Refs)

5. ULTRASOUND MONITORING OF LIVER METASTASES FROM COLORECTAL CANCERS (MEETING ABSTRACT).

Taylor RH, Gilbert JM, Evans MG, Lane HG, Cassell PG
Department of Gastroenterology, Central Middlesex Hospital, London, England
Gut; 22(5):A435 1981

Patients with liver metastases from colorectal cancer often receive chemotherapy. It is valuable in selecting patients and supervising their clinical condition to monitor the development and size of metastases. We report a prospective study using static greyscale ultrasound scanning to detect and measure liver metastases. Fifty patients with resected colorectal cancers had ultrasound scans as part of their routine follow-up at three monthly intervals for between three mo and four yr (median 15 mo). Scans were performed by one operator using a standard method on the same machine (Diasonograph NE4102, 3.5 MHz transducer). Half were receiving chemotherapy. Scans on nine patients were abnormal. Four had metastases shown on their first scan and five developed metastases during follow-up. Ultrasound detected these three to six mo before they were detectable clinically. Serial ultrasonic measurements of tumor size increased during follow-up. The remaining scans on 41 patients were normal and these patients continue to be well clinically. Tumors were graded at surgery and pathologically on a modified Dukes's classification. None of the four Dukes's A patients, 1/18 Dukes's B, 4/22 Dukes's C, and 4/6 Dukes's D have developed hepatic metastases. Ultrasound appears to be a simple, non-invasive method of early detection and monitoring of hepatic metastases from colorectal tumors. (no Refs)

6. COLON CARCINOMA SUBSEQUENT TO COLONSCOPIC REMOVAL OF NONINVASIVE (SURFACE) CARCINOMA (MEETING ABSTRACT).

Korn ER
Gastroenterology Division, Bay General Community Hospital, Chula Vista, CA
Gastroentest Endosc; 27(2):124 1981

Experience with colonoscopic polypectomies has lead to the widely held belief that if malignant changes are confined to the mucosa, without invasion of the stalk, simple polypectomy is curative. In this case a transcolonoscopic cecal polypectomy was performed, the polyp demonstrating surface carcinoma. Multiple sections demonstrated no evidence of neoplastic invasion beyond the muscularis mucosae. One yr subsequent to this procedure hemocult positive stools were noted. Colonoscopic examination at that time demonstrated a multilobular, sessile, polypoid lesion in the same area as the previously removed polyp. Biopsies of this lesion demonstrated well-differentiated adenocarcinoma later documented to be invasive via surgery.

Repeat pathological examinations of the original polyp with multiple new sections still failed to reveal any extension of the carcinoma through the muscularis mucosae. Colonoscopic identification of the same location of these lesions was facilitated by the fact that they were both immediately adjacent to the ileocecal valve. Although it may be argued that these were different lesions adequate localization was reasonably possible and they appeared to have been the same lesion. This report does not recommend that all patients should have a colonic resection for all adenomatous polyps demonstrating carcinoma in situ, but rather professes a caveat that occasionally a case may be found where simple polypectomy is not curative and, therefore, patients who have had colonoscopic polypectomy for localized carcinoma should be followed carefully. (no Refs)

7. ROLE OF COLONOSCOPY IN PATIENTS WITH UNEXPLAINED MELENA: ANALYSIS OF 53 PATIENTS.

Tedesco FJ, Pickens CA, Griffin JW, Sivak MV, Sullivan BH

Section Gastroenterology, Dept. Medicine, Medical Coll. Georgia, Augusta, GA, 30901

Gastrointest Endosc; 27(4):221-223 1981

Colonoscopy revealed significant pathologic conditions in 16 (30%) of 53 patients who presented with melena and had negative or nondiagnostic upper and lower gastrointestinal x-ray studies and negative upper endoscopy. (Author abstract) (8 Refs)

8. A NEW 30 CM FLEXIBLE SIGMOIDOSCOPE FOR THE MORE EFFECTIVE CONTROL OF LARGE BOWEL CANCER BY NON-ENDOSCOPISTS (MEETING ABSTRACT).

Winawer SJ, Andrews M, Cummins R, Ptak A

Dept. of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY

Gastroenterology; 80(5,part2):1316 1981

Fecal occult blood testing and proctosigmoidoscopy are considered to be the potential major screening techniques of large bowel cancer. Proctosigmoidoscopy has not enjoyed wide acceptance among physicians and patients because of discomfort, poor consistent insertion depth and high false-negativity. Control of large bowel cancer could possibly be enhanced by a 30-35 cm flexible sigmoidoscope (FS) for use by the non-endoscopist primary care physician. A 30 cm FS prototype provided by ACMI has been under evaluation. Patients are examined in the left lateral position. Family practice physicians and a nurse practitioner have been trained by observation, model instruction and supervision, followed by independent examinations. To date 314 patients have been examined independently with excellent patient comfort, enthusiastic examiner application, no risk and consistently good insertion depth. In this initial experience examinations were performed in less than 10 min in 286/314 pts (91%), and insertion was between 25 and 30 cm in 245/314 pts (78%). This preliminary experience has demonstrated the feasibility of the 30 cm flexible sigmoidoscope in the hands of non-endoscopists. This has encouraged expanded evaluation within the Strang Clinic screening setting, as well as the initiation of a multicenter national trial. The objectives are to further demonstrate the feasibility of this instrument as a replacement for the rigid sigmoidoscope for the more effective control of large bowel cancer. (no Refs)

9. COLONIC POLYPECTOMY, ITS ROLE IN CANCER PREVENTION (MEETING ABSTRACT).

Nagy GS, Fevre DI

Department of Gastroenterology, Royal North Shore Hospital, Sydney, Australia

Gastroentest Endosc; 27(2):126 1981

Endoscopic polypectomy can and will eliminate potentially malignant, not yet invasive, or early invasive carcinomatous polyps with promise of cure, obviating the need for major bowel resection. A review of 1500 endoscopic colonic polypectomies including 810 adenomatous polyps is presented. A significant risk of potential malignancy of polyps is evident. Significant dysplasia, ie cells showing malignant characteristics without evidence of invasion occurred in 17%, 31% and 26% in under 1 cm, between 1-2cm and over 2 cm size polyps respectively. Invasive carcinoma was found in 1%, 10% and 25% in the above three groups. Further supporting evidence for the 'polyp cancer sequence' is found in the increase in mean age from 56.37 yr in patients with benign adenomatous polyps to 60.66 yr in those with dysplastic polyps to 62.95 yr in the group with invasive carcinomatous polyps. There is also a direct relationship between the tubular, tubulo-villous and villous adenomas and size of polyp and also to the progression to dysplasia or carcinoma. Out of a total of 170 patients with significant dysplastic or early invasive carcinomatous polyps 154 did not undergo operative resection as the endoscopic polypectomy was deemed as adequate therapeutic measure. Over the 8 yr since these first came under surveillance none developed any local or metastatic carcinomas. From the evidence at hand, the outstanding value of endoscopic polypectomy in the detection and cure of early colonic cancer is well demonstrated. (no Refs)

10. A PRACTICAL SOLUTION TO THE DIAGNOSIS AND TREATMENT OF COLORECTAL CANCER? (MEETING ABSTRACT).

Farrands PA, Griffiths RL, Britton DC

Royal United Hospital, Bath, England

Gut; 22(5):A435 1981

If early colonic tumors bleed, fecal occult blood estimation of the asymptomatic populace may prevent 20,000 deaths annually, and eliminate the morbidity of colonic cancer surgery. A well-publicized prospective trial was undertaken in the single-practice market town of Frome, Somerset. Each of the 9050 townspeople aged over 40 yr received an envelope containing a personal letter of explanation, three Hemoccult test slides, and an instruction sheet. Completed slides were returned by 1817 people, 59 with positive tests were examined and endoscoped in a special clinic. Barium enema was arranged when indicated and hemorrhoids treated with sclerotherapy. One patient had colitis, six had severe diverticulosis, and 25 had perianal conditions which can bleed. Twenty-one had no clinical or radiological abnormality and are still under review. Six had colorectal neoplasms, four benign and two malignant. Three more patients in Frome presented with colonic tumors during the study. Two had refused to comply with the protocol because of cancerphobia; the third had been negative in the trial. Mass occult blood screening does detect asymptomatic colonic neoplasms, but a sympathetic national publicity campaign is required to increase the compliance if this method is to achieve its optimum potential. (no Refs)

11. THE FREQUENCY, APPEARANCE AND CLINICAL SIGNIFICANCE OF MACROSCOPIC CHANGES ASSOCIATED WITH DYSPLASIA AND CARCINOMA (MADC) COMPLICATING CHRONIC ULCERATIVE COLITIS (CUC) (MEETING ABSTRACT).

Butt JH, Konishi F, Morson BC, Lennard-Jones JE, Ritchie JK
St. Mark's Hospital, City Road, London EC, England
Gastroenterology; 80(5,part2):1119 1981

MADC have been proposed as markers for neoplastic complications of CUC. We analyzed the available colectomy material in the St. Mark's Hospital Registry to determine the clinicopathological characteristics of these changes. Thirty-four cases of cancer complicating CUC, 28 cases of severe dysplasia in CUC, 32 cases of CUC without dysplasia or cancer, and 77 cases of colorectal cancer were reviewed for micro and macroscopical changes. Four macroscopical lesions were described: polypoid lesions, low elevated lesions, strictures, and ulcers. In both categories there was a significantly greater proporton of Dukes' A cases in polypoid than in ulcerating cancers. There was a significantly greater number of cancers in low elevated lesions and in strictures in CUC than in cancer cases without CUC. More cancers occurred in the right and transverse colon and fewer in the rectum and sigmoid colon in CUC than in cases without CUC. Nineteen/thirty-four cases of cancer in CUC had a preoperative diagnosis of cancer based on macroscopic change; 5/19 were Dukes' A cases; 9/34 cases of cancer in CUC were operated because of severe dysplasia in flat mucosa: 6/9 were Dukes' A cases; this difference in proportion of Dukes' A cases was significant. Cancer in CUC has different macroscopical characteristics than colorectal cancer in patients without CUC. Clinical detection of these macroscopical changes yields a high proportion of cancers at colectomy. Detection of severe dysplasia in flat mucosa in contrast yields a significantly lower proportion of cases with cancer, which have a significantly greater proportion of Dukes' A cancers with greater likelihood of cure. (no Refs)

12. AMEBIASIS AND CARCINOMA OF THE LARGE INTESTINE - PATHOLOGICAL OBSERVATIONS AND CLINICAL ANALYSIS OF 21 CASES.

Xu C
Dept. Pathology, Hangzhou Tumor Hosp., Hangzhou, People's Pepublic of China
Zhonghua Neike Zazhi; 20(3):141 1981

Pathological and clinical findings are described for 21 cases of large intestinal amebiasis complicated with cancer of the large intestine. This series constituted 37% (21/57) of large intestinal amebiasis and 1.02% (21/2,051) of large intestinal cancer cases seen between 1963 and 1978. Tumors were primarily located in the rectum (18 cases) and the recto-sigmoid junction (3 cases). Histologically, 20 were well-differentiated adenocarcinoma and 1 was poorly-differentiated adenocarcinoma. Amebic protoplasm (nutrient body) was observed on and around the tumor nest. The relationship between amebiasis and intestinal cancer is discussed. (no Refs) (In CHI)

13. ELECTRON MICROSCOPY OF POLYPS OF THE COLON: II. INCLUSION BODIES OF LEUCHTENBERGER.

Balazs M
Dept. Pathology, Janos Hosp., Diosarok u. 1, H-1125 Budapest, Hungary
Exp Pathol; 19(3):164-171 1981

The electron-microscopic characteristics of the Leuchtenberger's inclusion bodies were studied in adenomatous, papillary and adeno-papillary polyps of the colon. According to them, formation of intracellular inclusions is due to focal cytoplasmic degradation, and that of intercellular inclusions to the herniation of the cytoplasmic part of epithelial cells. The formation of inclusions is believed to be connected with the low stage of development of the plasma membrane of rapidly proliferating undifferentiated colonic epithelial cells. During malignant transformation of polyps, the frequently occurring inclusions are considered an important morphological sign. (Author abstract) (9 Refs)

14. A SCANNING ELECTRON MICROSCOPY STUDY OF ULTRASTRUCTURAL CHANGES IN THE COLONIC MUCOSA OF PATIENTS WITH LARGE BOWEL TUMOURS.

Traynor OJ, Costa NL, Blumgart LH, Wood CB
(c/o Wood), Hammersmith Hosp., London, England
Br J Surg; 68(10):701-704 1981

Scanning electron microscopy (SEM) has been used to compare the appearance of th e colonic mucosal surface and overlying mucus layer of patients with normal colons, adenomatous polyps and colorectal carcinoma. The normal colonic mucosa had a characteristic orderly arrangement of crypts and was completely covered by an intact mucus layer. Epithelial and cryptal irregularities were seen on the surface of both polyps and carcinomas, and, in addition, the mucus layer was fragmented, leaving areas of the underlying epithelium exposed. These changes were more marked in colorectal cancers than in polyps and were present to a lesser degree in the apparently normal mucosa adjacent to tumors. The findings indicate that SEM can detect minor subtle irregularities on the surface of the colon and so may be useful in detecting pre-neoplastic and early neoplastic changes. (Author abstract) (23 Refs)

15. LOCALIZATION OF EARLY RECURRENCE OF CARCINOMA OF THE COLON OR RECTUM BY RADIOIMMUNODETECTION IN PATIENTS WITH A RISING SERUM CARCINOEMBRYONIC ANTIGEN CONCENTRATION (MEETING ABSTRACT).

Begent RH, Keep PA, Searle F, Dent J, Bagshawe KD, Jones BE, Jewkes RF, Vernon P
Department of Medical Oncology, Charing Cross Hospital, London, W6 8RF, England
Oncodev Biol Med; AbstractsBook,1:P62 1981

Radioimmunodetection (RID) for localization of carcinoma of the colon or rectum by external scintigraphy after injection of 131 Iodine labelled antibody to carcinoembryonic antigen (CEA) has been reported. The purpose of this study was to investigate whether the method could be used to localize recurrence of carcinoma of the colon and rectum which have been predicted by rises in concentration of serum CEA during follow-up after apparently curative resection. RID was performed using the method of Goldenberg in 10 patients with raised serum CEA in the absence of symptoms or physical signs of recurrence. RID was positive in 9, the sites being liver alone, 3; liver and para-aortic nodes, 1; liver and retrovesical area, 1; liver and colon, 1; perineum, 1; bone, 1; para-colic area, 1. These recurrences have been confirmed unequivocally in 4 patients. While recurrence is likely *in the remaining* 5 patients it has not been definitely demonstrated by conventional radiology or surgery. These preliminary data suggest that RID may be useful in the investigation of patients in whom subclinical recurrence of carcinoma of the colon or rectum is suspected. In its present form it can be used to indicate which sites of suspected recurrence should be further investigated. (1 Ref)

16. PREOPERATIVE SERUM CEA CONCENTRATION AND CLINICAL STAGING AS PROGNOSTIC FACTORS IN COLORECTAL CANCER (MEETING ABSTRACT).

Staab HJ, Brummendorf T, Anderer FA

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Oncodev Biol Med; AbstractsBook,1:61 1981

Most of the earlier investigations on the prognostic value of the preoperative s erum carcinoembryonic antigen (CEA) concentration in cancer patients examined its correlation with disease recurrence. In this report observed survival time was computed for 563 patients registered for resection of colorectal cancer since 1974. Significant difference in the survival rate was found for patients with different resectability, with different tumor extension and with different ranges of preoperative serum CEA concentrations. In addition, preoperative CEA concentration represented a significant gain in prognostic information within groups of patients with distinct resectability or/and tumor extension. The results indicated strongly that the preoperative serum CEA concentration seems to be an independent prognostic criterion within a group of clinically defined patients with comparable resectability and identical tumor, node, metastasis classification of their tumors. Therefore preoperative CEA determination, which can be established within about 10 days during hospitalization for primary treatment, should be included in clinical methods to give further information on patients with high risk. (no Refs)

17. MUCIN COMPOSITION AND CEA CONTENT IN ASSESSING MALIGNANT POTENTIAL OF COLONIC ADENOMAS (MEETING ABSTRACT).

Filipe MI, Abbas S, Greaves P

Department of Histopathology, Westminster Medical School, London, England

Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

Adenomas are considered precursors of colo-rectal cancer yet no precise marker exists for assessing their malignant potential. We studied the variations in the composition of mucus secretion and the presence of carcinoembryonic antigen (CEA) in 74 colonic adenomas (from patients with and without synchronous colonic cancer), 22 carcinomas and adjacent 'Transitional' (Tr) mucosa. We found A) as in normal a high proportion of O-acylated sialomucins in 'Tr' mucosa and benign adenomas but its absence in polyps with malignancy and in carcinoma; and B) a progressive increase in CEA from low in 'Tr' mucosa, raising with dysplasia in adenomas to a max in carcinoma. These changes were similar in both incidental and synchronous adenomas and related to dysplasia. All controls, including normal mucosa, 8 inflammatory and 7 metaplastic polyps showed high levels of O-acylated sialomucins and minimal or absent CEA except in the metaplastic polyps where CEA was seen. These *changes may* be an expression of abnormal maturation or early malignant transformation and prove useful as complement to the histological criteria of premalignancy. Furthermore, they illustrate the progression of change from a pre-adenomatous state to adenoma and malignancy. (no Refs)

18. THE EXPANDING FIELD OF COLORECTAL CANCER MARKERS: CEA, THE PROTOTYPE.

Zamcheck N

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Cancer Bull; 33(4):141-151 1981

Carcinoembryonic antigen (CEA) is the sole established marker for colorectal cancer. CEA is not specific to colorectal cancer or to cancer in general. CEA measurements appear to monitor experimentally induced changes in cultured human colon cancer cells just as they monitor changes in a patient's clinical course. Several molecules similar to CEA exist. Non-CEA-like antigens are increasing in number. The use of serial CEA determinations is the principal method for following a patient's clinical course, serves as one indication of successful or incomplete resection of colorectal cancer, gives evidence of recurrence, is useful in monitoring the effect of chemotherapy or radiation therapy and in decision-making to alter therapy, and provides a useful estimate of prognosis. Plasma CEA level provides a useful but not absolutely quantitative index of tumor mass and spread. Variability in plasma CEA levels is a result of many factors, including the marked variation in CEA produced by colonic tumor cells and in the amounts produced by primary colon cancer and metastases. The role of the liver in regulating CEA levels is discussed. Histopathologic evidence of tissue CEA production by positive tissue immunofluorescence or immunoperoxidase staining is regularly found in well-differentiated colorectal adenocarcinomas. Other topics discussed include tissue differentiation and preoperative CEA levels in prognosis and stratification, CEA activity in other body fluids, radioimmunodiagnosis, thermolabile polypeptide of CEA, serum galactosyltransferase isoenzyme, colon mucoprotein antigens, zinc glycinate marker, and combinations of markers. (140 Refs)

19. IMMUNOHISTOCHEMICAL EVIDENCE OF PEPTIDE HORMONES IN ENDOCRINE TUMORS OF THE RECTUM.

Alumets J, Alm P, Falkmer S, Hakanson R, Ljungberg O, Martensson H, Sundler F, Tibblin S

Dept. Histology, Univ. Lund, Biskopsgatan 5, S-223 62 Lund, Sweden

Cancer; 48(11):2409-2415 1981

Twenty-five endocrine tumors of the rectum (rectal carcinoids) were examined immunohistochemically for various pancreatic and gut neurohormonal polypeptides. Twenty-one of the tumors were found to contain cells displaying pancreatic polypeptide (PP), glucagon, somatostatin, insulin, substance P, enkephalin or beta-endorphin immunoreactivity. At least 11 of the tumors contained more than one peptide hormone. In some of the tumors PP cells made up the major cell population, in others the glucagon cells constituted the majority. Only four of the tumors contained 5-hydroxytryptamine. Rectal endocrine tumors seem unique among gut endocrine tumors in that they may store immunoreactive *enkephalin, beta-endorphin* and even insulin. None of the patients displayed the carcinoid syndrome; symptoms were usually vague and uncharacteristic. In many cases the tumor was found at routine examination. (Author abstract) (37 Refs)

20. MODIFIED PROTEIN KINASE ACTIVITY AND ISOZYME DISTRIBUTION IN ADENOCARCINOMA OF THE HUMAN COLON.

Raul F, Launay J-F, Galluser M, Doffoel M, Marescaux J, Grenier JF
Unite 61, INSERM, Ave. Moliere, Strasbourg Hautepierre, France
Biomedicine [Express]; 35(3):98-100 1981

Protein kinase activity and histone kinase isozyme distribution have been determined in soluble extracts of adenocarcinoma of the human colon and compared to adjacent normal mucosa. The results show an enhancement in endogenous protein kinase activity and the presence of an additional isozyme (PKI) for histone kinase activity in the tumor tissue. PKI activity exhibited a peculiar behavior in comparison to the isozyme. PKII present in both carcinoma and normal mucosa after dialysis of the soluble extracts. It is suggested that alteration of intracellular regulatory processes involved in PKI activity might be related to the maintenance of the proliferate state in human colon carcinoma. (Author abstract) (16 Refs)

21. BREATH METHANE EXCRETION IN PATIENTS WITH UNRESECTED COLORECTAL CANCER (MEETING ABSTRACT).

Karlin DA, Jones RD, Stroehlein JR, Mastromarino AJ, Potter GD
Dept. of Medicine, Gastroenterology Section, M. D. Anderson Hospital and Tumor Institute, Houston, TX, 77030
Gastroenterology; 80(5,part2):1188 1981

Eighty percent of patients with unresected colorectal (CR) cancer were reported to excrete greater than lppm breath methane (CH(4)) compared with 40% of a control group. Aim: To increase the data base and confirm the finding of our pilot study that there is no difference between control and CR cancer patient populations. Method: Patients had unresected CR cancer and had not had enemas for at least 7 days. Controls included patient spouses, relatives, and hospital employees without known gastrointestinal diseases, who had not used enemas for a least 30 days. End-expiratory breath samples were analyzed for CH4 using gas chromatography. A breath methane excretor (CH(4)+) was defined as greater than lppm CH4 above ambient levels. Results and Conclusions: There is no significant difference in the frequency and amount of breath CH4 excretion in patients with unresected CR cancer and control subjects. There is no relationship between the anatomic location of the unresected CR cancer and breath CH4 excretion. There is no relationship between age and breath CH4 excretion. Under the conditions of this study the analysis of breath CH4 does not appear to be promising for identifying asymptomatic individuals at increased risk for developing CR cancer. (2 Refs)

22. ANTITHROMBIN III PROFILES IN MALIGNANCY, RELATIONSHIP TO PRIMARY TUMORS AND METASTATIC SITES.

Honegger H, Anderson N, Hewitt LA, Tullis JL
(c/o Tullis) Dept. Medicine, New England Deaconess Hosp., Boston, MA, 02215
Thromb Haemost; 46(2):500-503 1981

Variations in antithrombin III (AT III) were correlated with origin of tumor, tumor spread, and localization of metastases in 118 patients with tumors (breast 34, lung 25, colon 19, lymphoma 15, ovary 12, pancreas 6, prostate gland 7) and in 247 normal controls. AT III was studied by standard clotting (functional) assays and protein concentration was examined by an immunodiffusion technique. The mean AT III functional level of all tumors was 28.60 +-16.63 sec vs 35.43 +-12.74 sec for controls; in 112 patients immunologic AT III was also lower than normal. AT III deficiency was more common in patients with cancer of the colon, ovary, and prostate than in those with other common tumors. AT III was lower in patients with local spread and metastases compared with those in remission. In 33 patients with proven liver metastases, functional AT III was reduced to av 23.3 sec and was correlated with reduction in serum albumin. The correlation coefficient (R) for functional and immunologic AT III in a blood sample from a given patient was approx 0.3 in controls; R increased in certain tumors, reaching greater than 0.5 in metastatic tumors and 0.72 in lymphoma. The implications of low AT III are not fully understood. (19 Refs)

23. SERUM CERULOPLASMIN LEVELS IN SURGICAL CANCER PATIENTS: RELATIONSHIP WITH TUMOR STAGE AND POSTOPERATIVE COMPLICATIONS (MEETING ABSTRACT).

Dionigi P, Dionigi R, Pavesi F, Mazari S, Goggi D
Istituto di Palologia Chirorgica, Universita di Pavia, Pavia 1-27100, Italy
Eur Surg Res; 13(1):31 1981

The purpose of this study is: (1) to evaluate serum ceruloplasmin (CP) in surgical patients with different types of neoplasias; (2) to analyze the possible relationship between CP levels and age, sex and tumor stage; (3) to determine the relative value of preoperative CP to identify cancer patients with higher risk of postoperative septic complications. CP has been evaluated at admission in 109 surgical cancer patients (48 males, 61 females, mean age 57 yr) divided in 5 groups: breast, melanoma, lymphoma, esophagus-stomach, sigma-rectum; 33 controls (27 males, 6 females, mean age 41 yr) were normal subjects or patients with minor surgical benign lesions. Tumor-stage (I-IV) was evaluated following International Union Against Cancer classification. Patients were defined septic if they presented after surgery a diagnosed focus of infection or if they had an undiagnosed fever for at least 3 days. CP has been evaluated by single radial immunodiffusion technique. Cancer patients presented significantly higher values of CP than controls. Minor differences were observed in melanoma, whereas CP was more significantly increased in breast, esophagus-stomach, sigma-rectum, and lymphoma. CP did not correlate with sex and age within the 5 groups considered; on the contrary a positive correlation was found with tumor stage. I n fact, the lower levels of CP were observed in patients at stage I, intermediate values at stage II and III, and higher values at stage IV. The results of this study show a positive relationship between CP and tumor progression suggesting that variations of CP may have an important clinical value for the evaluation of the diffusion of different neoplasias. (no Refs)

24. VITAMIN TITERS IN PRIMARY COLON ADENOCARCINOMA (MEETING ABSTRACT).

Frank O, Chen T, Baker H
Department of Medicine, New Jersey Medical School, East Orange, NJ
Am J Clin Nutr; 34(4):637 1981

The vitamin requirements of tumors may provide a clue to the use of antitumor agents, other than antifols, which could antagonize growth by interfering with tumor metabolism at a site other than nucleic acid synthesis. This promoted us to study vitamin titers in human colon adenocarcinoma to ascertain whether this tumor type had the increased vitamin requirements hypothesized as demanded for its increased growth. Twenty-four samples of human colon adenocarcinoma obtained at surgery, and uninvaded colon tissue adjacent to the tumor site, were analyzed for vitamin B12, vitamin B6, niacin, riboflavin, thiamin, biotin, pantothenate, folate, and biopterin activity. All patients were males, 50-70 yr old, eating a hospital diet; non had received therapy for treatment of the primary tumor. Human colon adenocarcinoma contains 1.8-3.5 more of all the above vitamins as compared to normal adjacent colon tissue with the exception of vitamin B12 which was at half-concentration in the tumor. The heightened vitamin titers in colon adenocarcinoma suggest the use of vitamin antagonists as possible inhibitors of colon adenocarcinoma. (no Refs)

25. CYTOLYTIC ULCERATIVE COLITIS-SPECIFIC SERUM ANTIBODY: ANTIGENIC RECOGNITION OF COLON CANCER CELLS AND RELATION TO DISEASE STATE (MEETING ABSTRACT).

Das KM, Tamura M, Nagai T
Albert Einstein College of Medicine, Bronx, NY, 10461
Gastroenterology; 80(5,part2):1132 1981

Using the antibody dependent microcytotoxicity (ADCC) assay, we have studied sera of patients with ulcerative colitis (UC) for antigenic recognition of 3 cancer cell lines, RPMI-4788, HT-29 and SW-1417. HeLa cells with the same HLA type as the RPMI-4788 served as controls. Peripheral blood mononculear cells from healthy subjects were used as effector cells. Cytotoxicity (CTX) was expressed as percent of specific 51Cr release after 4 hr of incubation with serum. Control experiments with aggregated human IgG, a monospecific anti-HLA-2 antibody and Escherichia coli 0:14 or 0:11 antigens, demonstrated specific Fc receptor binding for ADCC and the UC-serum antibody is most likely not related to HLA or the bacterial antigens. Sera from patients with active UC showed CTX against each of the 3 colon cancer cell lines. Absorption o f serum with each cell line decreased or abolished CTX against the other 2 lines. Absorption with HeLa cells left CTX against cancer lines intact. Sera from each of the 14 patients with active UC demonstrated CTX, but only 6 of 22 patients in remission showed CTX. Sera from patients with active Crohn's disease, rheumatoid arthritis and systemic lupus erythematosus did not show CTX. CTX disappeared 3 mo after total colectomy in 4 patients with active UC previously. These results suggest that the serum of patients with active UC recognizes a common antigen(s) in the 3 colon cancer cell lines. The cytolytic process demonstrated in vitro may be a factor in the pathogenesis of UC. (no Refs)

26. LYMPHOCYTE REACTION IN LYMPH NODES AND ITS EFFECT ON RECTAL ADENOCARCINOMA PROGNOSIS.

Chen Z, Ding C, Zheng S, Zhou X, Xu B
Dept. Pathology, Shanghai Second Medical Coll. Affiliated Ruijin Hosp.,, Shanghai, People's Republic of China
Zhonghua Yixue Zazhi; 61(3):136-138 1981

Lymphocyte reactions in lymph nodes are described in relation to prognosis for 488 cases of rectal adenocarcinoma that had been followed between 1958 and 1977. Based on pathologic examination of surgical specimens, degree of lymphocyte reactions and interstitial lymphocyte infiltration, follicular hyperplasia and sinus histiocytosis in adjacent lymph nodes, and analysis of postoperative survival rates, it was found that prognosis was good in cases with marked lymphocyte reaction in lymph nodes and in those patients with marked lymphocyte follicular hyperplasia and sinus histiocytosis in adjacent lymph nodes. Prognosis was poor in cases with poor lymphocyte reactions. It was concluded that host immune reactions play an important role in the prognosis of rectal adenocarcinoma. In order to obtain a better and overall understanding of patient prognosis, it is suggested that the host-cancer immune status be examined during routine pathological observation. (6 Refs) (In CHI)

27. INCREASED CIRCULATING TALPHA LYMPHOCYTE POPULATION IN BRONCHOGENIC AND COLONIC CARCINOMA.

Pucci A, Clancy RL, Doe WF
Dept. Medicine, Royal North Shore Hosp., St. Leonards 2065, New South Wales, Australia
Clin Exp Immunol; 46(1):130-133 1981

The proportion of T lymphocytes bearing membrane receptors for IgA (Talpha cells) was markedly increased in the peripheral blood of patients suffering from cancers of the colon and bronchus compared to an age-matched normal population and to age-matched control patients being treated for non-malignant chronic inflammatory conditions of the intestine and lung. By contrast, the percentage of the T lymphocyte population having Fc-IgG receptors (Tgamma cells) and Fc-IgM receptors (Tmu cells) in mucosal malignancy was similar to that found in the two control populations. It is suggested that the increased percent age of Talpha cells found in colonic and bronchogenic carcinoma patients may reflect an as yet unknown regulatory function for this subset. (Author abstract) (7 Refs)

28. DOES PROXIMITY TO COLORECTAL CARCINOMA SUPPRESS THE IMMUNOLOGICAL COMPETENCE OF LYMPHOCYTES? (MEETING ABSTRACT).

Hutchinson GH, Heinemann D, Symes MO, Williamson RC
Department of Surgery, Bristol Royal Infirmary, Bristol, England
Gut; 22(5):A422 1981

The finding that lymphoreticular infiltration of solid tumors may impart a favorable prognosis prompted a study of lymphocyte immunoreactivity in human colorectal cancer. Tumor digests (collagenase/DNAse) from 16 large-bowel carcinomas were passed through a nylon-wool column to separate neoplastic cells and tumor infiltrating lymphocytes. Lymphocytes were also obtained from the peripheral blood by centrifugation on a Ficoll-Isopaque gradient. The cytotoxicity of each population of lymphocytes was assayed against autoplastic tumor cells, using a two hr 51Cr release assay. In 11 of 16 patients peripheral blood lymphocytes showed moderate cytotoxicity, whereas tumor infiltrating lymphocytes showed similar cytotoxicity in only five cases. The cytotoxicity of tumor infiltrating lymphocytes from 11 patients was therefore compared before and after washing six x in medium 199. Reactivity against tumor cells was shown by unwashed tumor infiltrating lymphocytes in three of 11 and by washed tumor infiltrating lymphocytes in nine (p less than 0.02). At effector: target ratios of 10:1 and 20:1 the level of reactivity was significantly greater for washed tumor infiltrating lymphocytes. The cytotoxicity of lymphocytes derived directly from the tumor may be impaired by a blocking factor (perhaps tumor-associated antigen), adherent to the lymphocyte membrane but removed by washing. Proximity to the carcinoma may suppress the immunological competence of lymphocytes. (no Refs)

29. DIFFERENTIAL IMMUNE REACTIVITY OF TUMOUR-INTRINSIC AND PERIPHERAL-BLOOD LYMPHOCYTES AGAINST AUTOPLASTIC COLORECTAL CARCINOMA CELLS.

Hutchinson GH, Heinemann D, Symes MO, Williamson RC
Dept. Surgery, Medical Sch., Univ. Walk, Bristol BS8 1TD, England
Br J Cancer; 44(3):396-402 1981

Peripheral blood lymphocytes (PBL) were obtained from 13 patients and tumor-intrinsic lymphocytes (TIL) from 20 patients with colorectal cancer. The PBL were separated on a Ficoll-Isopaque gradient and the TIL by digestion of the tumor with collagenase-DNase. Both PBL and TIL were passed through nylon-wool columns and the eluted cells were co-cultured for 2 hr with 51Cr-labelled tumor cells from the same patient. If patients in whom spontaneous 51Cr release from the tumor cells was greater than 33% were excluded, PBL showed cytotoxicity for the autoplastic tumor cells in 5/10 cases and TIL in 3/10 cases (NS). In 12 cases the cytotoxicity of the TIL was compared with that for TIL from the same tumor after the lymphocytes had been washed a further 6x in Medium 199. Three effector: target (E/T) ratios, 5:1, 10:1 and 20:1, were used. The proportion of effector populations showing cytotoxicity was 2/12 for unwashed TIL and 9/12 for washed TIL (p less than 0.006). At the 5:1 E/T ratio the level of cytotoxicity was not significantly greater for washed TIL, but at the 10:1 ratio washed TIL showed significantly more cytotoxicity (p less than 0.025). At the 20:1 E/T ratio, a comparison was possible in 15 cases and the washed TIL again showed greater cytotoxicity (p less than 0.001). (Author abstract) (22 Refs)

30. SUPPRESSOR T-LYMPHOCYTES WITHIN HUMAN COLON CANCER (MEETING ABSTRACT).

Pucci A, Doe WF
Department of Medicine, University of Sydney at Royal North Shore Hospital, St. Leonards, 2065 New South Wales, Australia
Gastroenterology; 80(5,part2):1254 1981

Although peripheral blood studies of cell mediated immunity have been conducted in colon cancer patients, the relevance of these findings to tumor development is unclear. Since suppression of immunity to colon carcinoma represents a potentially important mechanism for tumor growth, the central question is whether suppression of T-cell responses occurs within the cancer itself. Human colon cancers were therefore disaggregated by mechanical means involving mincing, sieving and passage through a glass bead column. The tumor-derived cell suspension was characterized and the constituent cell population separated by bovine serum albumin density gradients to yield fractions enriched for tumor cells, macrophages and lymphocytes. The T-lymphocyte population was purified by sedimentation after rosetting with sheep RBC. Suppressor activity was tested by mitogenic responses to phytohemagglutinin in co-cultures of tumor-derived cells and autologous peripheral blood lymphocytes. In 9 out of 10 separate experiments the tumor-derived cells suppressed the mitogenic response of blood lymphocytes by 30-90%. Fractionation of the tumor disaggregate into T- and non T-cell populations indicated that the suppressor activity was constantly present in the T-cell population. By contrast, the heterogeneous T-cell-depleted population was variable in its effect and on occasion, actually enhanced the response to mitogen. These data establish for the first time the existence of a dominantly suppressor T-cell population within human colon cancers, and encourage further study of the regulation of T-cell responses in this common disease. (no Refs)

31. SIGNIFICANCE OF SERUM IMMUNE COMPLEX ASSAY IN CANCER OF THE STOMACH AND COLON.

Kaneko H
Second Dept. Surgery, Yokohama City Univ., Sch. Medicine, Minami-ku, Yokohama 232, Japan
Rinsho Meneki; 13(Suppl2):100-108 1981

This study represents an attempt to measure the circulating immune complexes in patients with cancer of the stomach or large intestine by the erythrocyte-amboceptor (EA) rosette inhibition test. The serum immune complex level determined by this method showed a significant correlation with that measured by the binding to surface receptors of cultured lymphoblasts (Raji cells) and a significant inverse correlation with the serum complement level (CH50). It did not correlate with the phytohemagglutinin skin test or lymphocytic blastogenesis assay, whereas the IgG.FcR+ T cell percentage was low in patients showing a high serum level of immune complexes. Clinically, circulating immune complexes were demonstrated in 66.7% of untreated patients with gastric carcinoma and 82.5% of those with carcinoma of the colon, in contrast with 5.9% in normal controls. Of these patients, those who received a curative operation and those who underwent immunochemotherapy and/or local continuous ia infusion with anticancer drugs displayed a significant decrease in circulating immune complexes. The results indicate that serum immune complexes can be measured by the EA rosette inhibition test; that there appears to be no correlation between the serum immune complex level and nonspecific cellular immune responsiveness; and that the IgG.FcR+ T cell percentage is not correlated with the serum concentration of the immune complexes but the data obtained suggest the presence of immune complexes attached to IgG.FcR+ T cells. (26 Refs) (In JPN)

32. COST EVALUATION OF HEMOCCULT STOOL TESTING TO DETECT ASYMPTOMATIC COLORECTAL CANCER (MEETING ABSTRACT).

Feldman R, Allison JE
Kaiser-Permanente Medical Group, 280 W. MacArthur Blvd., Oakland, CA, 94611
Gastroenterology; 80(5,part2):1147 1981

A study was conducted in Oakland, California of 14,041 unselected Kaiser Health Plan members greater than or equal to age 45 who had multiphasic examinations (MHC) during a 12 mo period to evaluate the cost effectiveness of Hemoccult screening for colonic adenocarcinoma (AdCa). The Hemocult II slides were mailed prior to the MHC; 10,255 (70.3%) patients returned slides, and of these 112 (1.1%) were positive. A recommended protocol, including colonscopy, for the diagnostic workup of these patients was distributed to their physicians. Review of the medical records of patients with positive Hemoccult revealed 10 patients with AdCa. and 14 patients with colonic polyps greater than or equal to cm (some multiple). The av cost of detecting AdCa was 3,510 dollars/patient; and for AdCa and/or polyps greater than or equal to 1 cm 1,460 dollars/patient. A review of colorectal AdCa diagnosed in 1974 at the Oakland Kaiser Medical Center was done (1) to compare the Duke's staging to the present study, and (2) to determine the 5-yr costs for medical care for each stage. The av costs/person yr and av length of survival in yr according to Duke's staging were as follows: A, 1,320 dollars (6.7 yr); B, 1,960 dollars (4.7 yr); C, 4,620 dollars (2.8 yr); D, 16,760 dollars (0.6 yr). In this study, no significant difference was found in the staging detected by Hemoccult testing compared to previous yr without screening. If the assumption is made that polyps greater than or equal to cm are precancerous, a cost benefit can be shown for Hemoccult screening. (no Refs)

THERAPEUTIC MODES OF COLO-RECTAL TREATMENT

33. ABDOMINAL SACRAL RESECTION OF LOCALLY RECURRENT RECTAL CANCER.

Wanebo HJ, Marcove RC
Dept. Surgery, Univ. Virginia Medical Center, Box 181, Charlottesville, VA, 22908
Ann Surg; 194(4):458-471 1981

Local recurrence of rectal cancer develops in the posterior bony pelvis as an isolated event in about half of the patients with recurrence. Although radiation can palliate sacral root pain, the disease is usually progressive and is rarely amenable to conventional resection. We have adapted a surgical technique usually used for primary sacral tumors, which permits a complete en bloc excision of recurrent rectal cancer in most instances. This approach consists of a laparotomy with pelvic dissection and mobilization of structures to be resected. The patient is repositioned prone and the posterior pelvis (sacrum and side walls) is then resected with preservation of appropriate nerve roots of the posterior pelvis and the sciatic nerve. Reconstruction is done with muscle and skin flaps. We have done 21 such procedures, of which, 11 were for pelvic recurrence of rectal adenocarcinoma. Seven patients had resections for cure and four had palliative resections of fungating or infected tumors. All but one patient was postabdominal perineal resection and nine patients had been irradiated (3,000-9,000 rads). Two patients had received up to 9,000 rads in separate courses (external beam in one and interstitial radiation in the other). The posterior extent of resection was S1-2 to 5 in six patients; S3 to 5 in three patients, and S4-5 in two patients. Anterior exenteration was performed in three patients and three patients had additional resection of other organs. In the curative resection group, three patients are living free of disease at 6, 10, and 52 mo, and one patient was NED at 60 mo, but has again had tumor recurrence and is living with disease at 65 mo. One patient died of disease at 13 mo and one patient died of a pulmonary embolus following resection for ureteral obstruction at 5 mo. One postoperative death occurred from a cerebrovascular accident at 52 days. In the palliative resection group, three patients survived with relief of local tumor symptoms 4, 8, and 12 mo. One patient who had received a total of 9,000 rads developed flap necrosis, small bowel fistula and died 60 days after resection. although this is a small series, it suggests that abdominal sacral resection of locally advanced pelvic cancer is feasible and may provide good palliation in most and possible cure in some patients who develop recurrence and primary resection of adenocarcinoma of the rectum. (Author abstract) (no Refs)

34. THE CHANGING PATTERN AND THE CHANGING SURGICAL TREATMENT OF RECTAL CARCINOMA.

Shepherd JJ
Univ. Tasmania, Clinical Sch., 43 Collins St., Hobart, Tasmania 7000, Australia
Australas Radiol; 25(2):147-149 1981

Clinical aspects of rectal carcinoma are discussed and reviewed. Symptoms have shown little change over the yr, but more tumors are now found in the upper 1/3 of the rectum and fewer in the lower 1/3, compared with 25 yr ago. Malignant potential of villous adenomas, diagnosis of rectal carcinoma by clinical examination and endoscopy, need for a full blood count and nutritional assessment, and surgical management of rectal tumors are discussed. Of the approaches to radical surgery, sphincter-saving anterior resection is now preferred to abdomino-perineal resection. This trend is due to the increased incidence of tumors in the upper 1/3 of the rectum, increased knowledge of the anatomy and physiology of the anal sphincter, and introduction of stapling devices. (10 Refs)

35. EXPERIENCE WITH SINGLE-LAYER RECTAL ANASTOMOSIS.

Khubchandani M, Upson J
Dept. Surgery, State Univ. New York, Buffalo, NY
J R Soc Med; 74(10):736-738 1981

Anastomotic dehiscence following resection of the large intestine is a serious complication. Satisfactory results of single-layer anastomosis depend upon meticulous technique and a scrupulously clean colon. Out of 65 single-layer anastomoses involving the rectum, significant leakage occurred in 4 patients. The results are reported in order to draw attention to the safety and efficacy of one-layer anastomosis. (Author abstract) (8 Refs)

36. ELECTIVE SURGERY FOR ULCERATIVE COLITIS: COLECTOMY IN 158 PATIENTS.

Albrechtsen D, Bergan A, Gjone E, Nygaard K, Flatmark A
Surgical Dept., Rikshospitalet, Natl. Hosp., Oslo, Norway
Scand J Gastroenterol; 16(6):825-831 1981

Chronic ulcerative colitis was treated by elective colectomy in 158 patients. Proctocolectomy and ileostomy was performed in 140 patients and colectomy and ileorectal anastomosis (CIRA) in 18 patients. The operative mortality was 2.5%, and postoperative complications, mostly infections, occurred in 38%. Within a 2-yr postoperative period another 1.9% of the patients died, and late complications occurred in 18%. Colorectal carcinoma was present at the time of colectomy in 5.1% and developed some yr later in another two patients primarily operated on with CIRA. Half of the cancer patients died of malignancy. Most extracolic complications, present in 25% of patients before colectomy, regressed or disappeared after operation. Half of the patients operated on with CIRA needed to have their rectum removed within a few yr because of cancer or proctitis, and few of the rest had lasting relief of symptoms. (Author abstract) (26 Refs)

37. RESULTS OF RESECTION AND COLO-ANAL ANASTOMOSIS FOR CARCINOMA OF THE RECTUM (MEETING ABSTRACT).

Percy JP, Parks AG
St. Mark's Hospital, London, England
Gut; 22(5):A429 1981

Restorative resection is used increasingly for rectal carcinoma because it obviates the need for a permanent colostomy and is statistically as curative as total excision. However, where an anastomosis is technically difficult, alternatives to total excision are described but have not gained widespread acceptance. Since 1973, 75 patients with rectal carcinoma in a situation unsuitable for anterior resection have had sphincter function preserved by an overlapping sutured anastomosis performed within the anal canal from the perineal aspect. The results have been analyzed. The pathological characteristics of these tumors were comparable with those of all rectal carcinomas treated at St. Marks Hospital between 1948 and 1972. Two patients developed pelvic sepsis after colonic necrosis and anastomotic breakdown. Eight developed pelvic sepsis without major anastomotic breakdown. Four patients have developed recurrent pelvic tumor. Twenty-one of 32 patients are alive without sign of recurrence at three yr and 12 of 19 are alive five yr after a curative operation. Sixty-nine of the 70 patients whose colostomies had been closed at the time of assessment had normal or near normal bowel function. The operation is straightforward, has a morbidity and mortality comparable with alternative procedures, and produces good functional results. (no Refs)

38. HIGH-DOSE PENICILLIN TO PREVENT POSTOPERATIVE WOUND SEPSIS AFTER ILEOCOLORECTAL OPERATIONS.

Raahave D
Dept. Gastroenterological Surgery, Rigshospitalet, Univ. Copenhagen, Copenhagen, Denmark
Scand J Gastroenterol; 16(6):789-793 1981

Two hundred and twenty-two patients were admitted to a controlled trial to investigate the effect of penicillin in the prevention of postoperative wound infection after ileocolorectal operations. The study group was treated with 5 MIU of penicillin iv bid for 4 days, starting at operation, together with an intraincisional injection of penicillin at wound closure. The rate of wound infection was 11/93 (11.8%), compared with 15/92 (16.3%) in the control group, which was given a regimen of 2 MIU penicillin and 0.5 g streptomycin bid for 5 days; no difference existed between these sepsis rates (p greater than 0.05). Measurements of the operation wounds per- and post-operatively showed a mean infected wound length of 7.3 +-4.0 cm, this being only one third of the original wound length, and no difference existed between the two treatment groups. A rate of partial wound infections of 1 in 10 seems acceptable after ileocolorectal operations, especially when achieved by penicillin therapy, which is inexpensive and free of serious risks. (Author abstract) (26 Refs)

39. CONTROLLED COLOSTOMA WITH MAGNETIC CLOSING DEVICE.

Fedorov VD, Rykov VI, Blagodarnyi LA, Odariuk TS, Markova EV, Mukho SB
Res. Inst. Proctology, Moscow, USSR
Khirurgiia (Mosk); (8):91-94 1981

Functional efficacy of controlled colostoma with magnetic closing device was evaluated in 10 patients rectal carcinoma. All patients underwent abdominal-perineal extirpation of the rectum with colostomy and simultaneous implantation of magnetic rings into the thickness of the abdominal wall. All patients were able to retain the intestinal content. (7 Refs) (In RUS)

40. ENDOSCOPIC POLYPECTOMY: INADEQUATE TREATMENT FOR INVASIVE COLORECTAL CARCINOMA (MEETING ABSTRACT).

Colacchio TA, Forde KA
Department of Surgery, Columbia-Presbyterian Medical Center, New York, NY
Gastroentest Endosc; 27(2):133 1981

Endoscopic polypectomy has greatly decreased the necessity for transabdominal resection of adenomatous polyps of the colon and rectum. In addition, the routine removal of these presumed precancerous lesions may well decrease the incidence of colon cancer in these patients. At Columbia-Presbyterian Medical Center, we have reviewed 733 patients who have undergone endoscopic removal of pedunculated adenomatous polyps of the colon and rectum during the past decade. Forty-three (5.9%) of these patients had polyps containing carcinoma-in-situ for which no further resection was performed. Forty-seven patients (6.4%) had polyps containing carcinoma which had invaded up to or through the muscularis mucosa and were therefore considered invasive carcinomas. In this latter group, 31 patients underwent colon resection and 16 underwent endoscopic polypectomy alone. Within the group undergoing resection, eight patients (26%) had from one to two lymph nodes within the resected specimen containing metastatic cancer. In review of these lesions, all 31 were able to be resected with an intervening segment of uninvolved stalk. All patients with polyps containing invasive carcinoma should undergo standard colon resection if feasible, despite the technical ability to resect these lesions endoscopically with an 'adequate' margin of uninvolved stalk. This will eliminate the possiblity of undiagnosed Dukes' C lesions, and potentially improve our long-term survival with this group of patients with an otherwise poor prognosis. (no Refs)

41. PHASE I STUDY OF MISONIDAZOLE AND CYCLOPHOSPHAMIDE IN SOLID TUMORS (MEETING ABSTRACT).

Klein L, Presant CA, Vogel CL, Gams R, Johnson R

City of Hope National Medical Center, Duarte, CA, 91010

Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.

The combination of radiation therapy and misonidazole is currently being tested in the treatment of human solid tumors. Experimental data have suggested that the combination of misonidazole and systemic chemotherapy (such as cyclophosphamide and/or other alkylating agents) produces enhanced therapeutic effects. A Phase I study of iv cyclophosphamide and misonidazole has been designed to determine the dose-limiting toxicity and recommended therapeutic doses. Misonidazole is given at either of two dosage levels, 1 g/m2 or 2 g/m2 every three wk. Escalating doses of cyclophosphamide are given until dose-limiting toxicity is reached at each misonidazole dosage. Pharmacokinetics of cyclophosphamide and misonidazole are being studied. Five patients with advanced, refractory solid tumors have, to date, been treated in this ongoing study. Tumors treated have included metastatic breast cancer (2), colon cancer (1), small cell carcinoma of lung (1), and gastric cancer (1). All patients had received extensive prior chemotherapy and radiation therapy but had not received any therapy for a minimum of three wk. All patients to date have received misonidazole 1 g/m2. Six courses of cyclophosphamide 400 mg/m2 and two courses of cyclophosphamide 600 mg/m2 are evaluable. Three of eight courses were associated with mild nausea and vomiting lasting for two days. One patient had mild glossitis occurring two wk after treatment and lasting for five days. At a max total misonidazole dose of 2 g/m2 no patient has developed peripheral neuropathy, encephalopathy, or skin rash. No toxic deaths have occurred. At the present dosage levels, misonidazole may be given with cyclophosphamide without enhanced toxicity. (no Refs)

42. THE COMBINATION OF 5-FLUOROURACIL WITH MISONIDAZOLE IN PATIENTS WITH ADVANCED COLORECTAL CANCER (MEETING ABSTRACT).

Spooner D, Bugden R, Peckham MJ, Wist E

Radiotherapy Research Unit, Institute of Cancer Research, Sutton, Surrey, England

Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.

The observation that Misonidazole (MISO) substantially enhanced the cytotoxic effect of 5-Fluorouracil (5-FU) when given in combination in a murine tumor system with much less enhancement of bone marrow toxicity has led to a clinical pilot study of this combination. Ten patients with advanced colorectal cancer have been treated with 5-FU and MISO to assess the toxicity of the combination and to document any modification of MISO pharmacokinetics by 5-FU. 5-FU was given as an iv bolus (1.0 g/m(2)) at intervals of 3 wk; MISO was administered 4 hr before the second and subsequent courses in doses of 2 g/m2 (6 patients) and 3 g/m2 (4 patients) up to a cumulative dose of 12 g/m2. MISO plasma levels and weekly blood counts were monitored. A complete tumor response was seen in one patient and a second patient experienced a complete symptomatic response. Nausea and vomiting lasting between 4 and 24 hr was the major side effect observed, occurring in 18% of 5-FU courses; 44% 5-FU + MISO (2 g/m(2)) and 75% 5-FU + MISO (3 g/m(2)). Leucopenia occurred in 9.1% of 5-FU courses and 10.7% of 5-FU + MISO. No cases of diarrhea, stomatitis or peripheral neuropathy were seen in patients treated with the combination. The mean 4 hr plasma MISO level was 72.6 ug/ml (range 62-98) after 2 g/m2 and 87.9 ug/ml (57-123) after 3 g/m2 and the mean MISO half life was 13.0 hr (9.2-17 hr). Since these results are similar to previously published data for MISO administered alone, there is no evidence to suggest that 5-FU alters the pharmacokinetics of MISO. The results of this on-going toxicity study show that MISO and 5-FU can be combined safely and encourage us to consider a further trial of this combination in patients with advanced colorectal cancer. (no Refs)

43. PHASE II TRIAL WITH CHLOROZOTOCIN IN ADVANCED COLORECTAL CANCER.

Bleiberg H, Rozencweig M, Michel J, Clavel M, Longeval E, Feremans W, Bondue H, Lardinois J, Crespeigne N, Kenis Y

Service de Medecine et Laboratoire d'Investigation Clinique Henri Tagnon, Institut J. Bordet, 1 rue Heger-Bordet, 1000 Bruxelles, Belgium

Eur J Cancer Clin Oncol; 17(8):863-866 1981

The single agent activity of chlorozotocin was evaluated in advanced colorectal cancer not previously treated with chemotherapy. The drug was given at a dosage of 200 mg/m2 iv repeated every 6 wk. Of 23 evaluable patients, 2 achieved a partial response lasting 4 and 5 mo respectively. With this dosage regimen, chlorozotocin produced essentially nausea and vomiting in one-half of the patients as well as myelosuppression that varied with performance status. Our findings suggest that the therapeutic index of chlorozotocin is similar to that of other conventional nitrosourea derivatives in this disease. However, additional experience is needed to definitely assess how cumulative is their respective bone marrow toxicity. (Author abstract) (8 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLO-RECTAL NEOPLASMS

44. SIDNEY DOCTORS' KNOWLEDGE AND ATTITUDE ON COLORECTAL CANCER.

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Cancer Forum; 5(2):79-83 1981

Results of a survey on knowledge and attitudes of symptomatic colorectal cancer (CC) by a sample of metropolitan clinicians is reported. A 36 item questionnaire was sent to 760 doctors with 361 (47.5% response rate) replies obtained. The sample included general practitioners (GP; 49.6%), consultant physicians and general surgeons - including oncologists and gastroenterologists (12.2%), and physicians in other specialities (36.5%). Results show specialists to be most knowledgeable, approx 75% were involved with at least 1 diagnosed case compared with 50% of GP and 20% of the others. Specialists also gave more knowledgeable ansers on the incidence of CC (73% chose most or second most common form of cancer), overall 5 yr survival (48% were aware of 40% survival rate), and probability of new bowel cancer developing after successful resection of CC (75%). A majority of all three groups did not know that that sigmoidoscopy could visualize approx 40% of tumors. Most physicians also felt that earlier diagnosis of CC would lead to improved survival, while undergraduate teaching of early CC detection was rated as adequate by less than 50% of all groups. Diagnostic techniques included fecal occult testing (70% GP, 36% specialists, 22% others) and sigmoidoscopy (25% GP, 89% specialists, 10% others). While the difference in knowledge between specialists, GP and other physicians is understandable, a general knowledge of CC is desirable for doctors not working in this field as they provide a source of knowledge and reference for patients and their families. (2 Refs)

45. VILLOUS TUMORS OF THE COLON AND RECTUM.

Wang SM, Wei TC, Hsu SC, Chen KM, Wang CY

Dept. Surgery, Coll. Medicine, Natl. Taiwan Univ., Taipei, Taiwan

J Formosan Med Assoc; 80(5):509-518 1981

During a 12-yr period, 24 villous adenomas (14 malignant, 10 benign) were reviewed. These cases constituted 1.5% (24/1,598) of all colorectal polyps and 1.1% (14/1,270) of all colorectal cancers. The 15 males and 9 females ranged in age from 31-77 yr, with highest incidences in decades four and six. Sites included rectum 14, sigmoid colon 7, and one each descending colon, splenic flexure, and cecum. Most frequent symptoms were rectal bleeding and diarrhea. Duration of symptoms ranged from less than 3 mo (5 cases) to 4-5 yr (1 case). As to gross features, 12 were sessile, 8 pedunculated, 2 fragile, and 2 annular; the latter 4 were malignant. Av size of malignant tumors was 4.0 cm, benign tumors 2.6 cm. Histologically 5 were benign, 5 exhibited atypia, 10 carcinoma in situ and 4 invasive carcinoma. If there was no invasive carcinoma or the tumor was small, local excision was effective. In the presence of invasive or suspected invasive carcinoma, or the lesion was large, radical resection was performed. The local recurrence rate was 12.5%. Operative complications included hemorrhage (3), wound infection (2), colon perforation (1). For the series as a whole, 5-and 10-yr survivals were 88.9% (8/9) and 87.5% (7/8), respectively. (22 Refs)

46. MALIGNANT TUMORS AND OTHER UNUSUAL FEATURES ASSOCIATED WITH CARCINOID TUMORS OF THE GASTROINTESTINAL TRACT (MEETING ABSTRACT).

Kothari T, Mangla JC
University of Rochester Medical Center, Rochester, NY
Gastroenterology; 80(5,part2):1197 1981

The charts of 96 patients with gastrointestinal (GI) carcinoid tumors diagnosed over a 10-yr period at the University of Rochester Medical Center were reviewed and the associated malignancies and other unusual aspects analyzed. Forty-five patients had appendiceal, 31 ileal, eight rectal, three colon, two each of stomach duodenum jejunum and cystic duct. The potential for metastasis increases with increasing size of the tumors. All carcinoid tumors eventually will invade and metastasize except appendix. Surgical excision is the preferred mode of treatment. Even in patients with metastases, aggressive surgical approach prolongs the survival. Twenty-three associated malignant neoplasms were present in 17 patients which were mostly adenocarcinomas leading to an early death while the carcinoid tumors generally remained localized. While six colonic, two stomach, three endometrial, one pancreatic, two lungs, one prostatic carcinoma coexcised with carcinoid tumors of GI tract, carcinoma of rectum, ampulla, breast, brain, kidney and prostate developed in carcinoid patients one to seven yr later. There was 36% incidence of second malignant neoplasm in patients with ileal carcinoid, but no second tumor was found in patients with carcinoid of the rectum. Two patients presented with gallbladder disease and were found to have carcinoid tumors of the cystic duct. Three of the four patients with carcinoid syndrome died within two yr of the diagnosis. The presence of carcinoid tumor should alert the physician to search for a second malignant neoplasm. (no Refs)

47. IMMUNOBIOLOGY AND IMMUNOTHERAPY OF COLORECTAL CANCER.

Papermaster BW
Cancer Res. Center, Columbia, MO
Cancer Bull; 33(4):135-140 1981

Immunocompetence evaluation in colorectal cancer patients, immunotherapy protocols (strategy and results), and animal models and laboratory studies are presented. Although immunocompetence data are difficult to compare because of variation in study techniques, information increasingly indicates association of progressive immunodeficiency with advancing stage of disease. Some degree of immunodeficiency is already definable in a certain group of patients by the time they have Dukes' B disease. More consistent manifestation of immunodeficiency, particularly in the T-cell category, occurs as tumor progresses. The developmen of monoclonal antibodies and cytofluorometry should allow more precise categorization of T-cell defects. Increased peripheral blood immune responsiveness to ongoing colon cancer has been shown by leukocyte adherence inhibition (LAI). LAI has been correlated with tumor progression, development, and resection. Test results reflect alterations in the lymphoid system detectable by LAI and are correlated with progressive colon cancer. Results of immunotherapy trials suggest that advances in colon cancer therapy will occur at the adjuvant level, with immunotherapy acting as a supplement to established chemotherapeutic modalities rather than replacing them. Two animal model systems, the MCA38 mouse transplantable tumor and dimethylhydrazine treatment of rats, appear promising for the study of colon neoplasms. Analysis of lymphocyte populations and the use of monoclonal antibodies to colon carcinoma antigens are discussed. (34 Refs)

48. THE NATIONAL LARGE BOWEL CANCER PROJECT: OVERVIEW.

Copeland MM
M. D. Anderson Hospital and Tumor Inst., Univ. Texas, Houston, TX
Cancer Bull; 33(4):121-123 1981

Areas of research supported by the National Large Bowel Cancer Project are discussed. The incidence, diagnosis, and treatment of colon cancer are considered. Topics discussed in relation to large bowel cancer include the availability of suitable animal models, causation and biochemical control factors in cellular metabolism, relationship between diet and large bowel cancer, isolation and identification of mutagens/carcinogens resulting from cooking of meats and other products, chemotherapy and immunotherapy, colon cancer screening, and familial polyposis and Gardner's syndrome as models for colon carcinoma. (31 Refs)

49. MUCINOUS ADENOCARCINOMA DEVELOPING IN CHRONIC ANAL FISTULA: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE.

Getz SB, Ough YD, Patterson RB, Kovalcik PJ
Naval Regional Medical Center, Portsmouth, VA, 23708
Dis Colon Rectum; 24(7):562-566 1981

Mucinous adenocarcinoma developing in a chronic anal fistula is a rare tumor of the anus of which there are less than 150 reported cases. There has been some debate as to whether the fistula is the source of the tumor, or whether the fistula is the presenting feature of a slow-growing, indolent carcinoma. Two recent cases seen at our hospital are presented, along with a review of the literature and what we feel to be strong evidence that the fistula and associated anal glands are indeed the source of this unusual tumor. (Author abstract) (14 Refs)

50. THE ASSOCIATION OF CARCINOID TUMORS OF THE RECTUM WITH MYELOFIBROSIS: REPORT OF TWO CASES.

Nelson RL
Dept. Surgery, Univ. Illinois Hosp., Post Office Box 6998, Chicago, IL, 60680
Dis Colon Rectum; 24(7):548-549 1981

Two patients with myelofibrosis, a primary malignancy of the hematopoietic system, have developed carcinoid tumors of the rectum. This development is rare, as rectal carcinoids are more often associated with other carcinomas of the gastrointestinal tract. Rectal carcinoid tumors are, in general, less commonly associated with second malignancies than are carcinoid tumors of foregut and midgut origin. (Author abstract) (8 Refs)

51. INITIATION AND CHARACTERIZATION OF CULTURES OF HUMAN COLONIC CARCINOMA WITH DIFFERENT BIOLOGICAL CHARACTERISTICS UTILIZING FEEDER LAYERS OF CONFLUENT FIBROBLASTS.

Brattain MG, Brattain DE, Fine WD, Khaled FM, Marks ME, Kimball PM, Arcolano LA, Danbury BH
Dept. Biochemistry, Univ. Alabama, Birmingham, AL, 35294
Oncodev Biol Med; 2(5):355-366 1981

The effects of feeder layers of C3H 10T1/2 murine fibroblast cells on the establishment of cultures of human colonic carcinoma were determined for 27 tumor specimens. Of the 27 specimens, 21 were successfully established on feeder layers. All except for 1/21 have been sub-cultured at least 10 times and have been maintained in tissue culture for 6-12 mo. When feeder layers were not used only three specimens were able to grow and survive passage in culture. Of the 21 specimens grown in long-term cultures, 14 have been weaned from fibroblasts and characterized. These 14 lines were divided into three groups on the basis of their tumorigenicity in nude mice. Group 1 cells, in general, produced poorly differentiated tumors and had in vitro morphologies typical of the grape-like cluster or miscellaneous forms. Group 2 cells were less tumorigenic than Group 1 cells, they grew poorly or not at all in semi-solid medium and produced carcinoembryonic antigen (CEA) levels in the medium of confluent cultures that were indistinguishable from those of Group 1 cells. Tumors from Group 2 cells were differentiated and, in general, grew in an epithelioid pattern in vitro. Group 3 cells were, in general, not tumorigenic, produced large amounts of CEA, grew in the epithelioid pattern, and would not grow well in semi-solid medium. (28 Refs)

52. THE EFFECTS OF SODIUM BUTYRATE ON EPIDERMAL GROWTH FACTOR BINDING TO HUMAN COLORECTAL CANCER CELLS (MEETING ABSTRACT).

StHilaire RJ, Kim YS
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Gastroenterology; 80(5,part2):1267 1981

Epidermal Growth Factor (EGF), a 6000 mol wt protein hormone produced by salivary and Brunner's glands, has been shown to have a mitogenic effect in normal intestine. Work in our laboratory has demonstrated that EGF stimulates the growth of human adenocarcinoma cells in culture as well as binding to a 180,000 mol wt cell surface receptor. Sodium butyrate (NaBt) has been reported to induce differentiation in some cancer cell systems. In this study a human rectal carcinoma cell line (HRT-18) and a human colon adenocarcinoma cell line (HT-29), whose growth is stimulated by EGF, were grown in the presence of NaBt to assess alterations in growth, tumorigenicity, EGF receptor numbers and characteristics. NaBt treated cells in both cell lines exhibited longer doubling times, lower saturation densities, and an inability to demonstrate anchorage independent growth when compared with control nontreated cells. A significant increase in receptor numbers was noted when expressed as binding per well or binding per mg protein. HRT-18 demonstrated a two-fold increase while HT-29 demonstrated a 1.3 fold increase after incubation with 2mM NaBt. This increase appears to require protein synthesis. Gel filtration and lectin affinity chromatography suggested that the EGF-receptor complex is a glycoprotein. In summary, NaBt can cause changes in cell growth in human colon cancer cells, suggesting lower tumorigenicity, while at the same time causing quantitative changes in EGF receptors. (no Refs)

53. EFFECT OF TRANSFERRIN ON THE GROWTH OF A HUMAN RECTAL CANCER CELL LINE (MEETING ABSTRACT).

Morita A, Wong AD, Kim YS
Gastrointestinal Research Lab., Veterans Administration Medical Center, San Francisco, CA, 94121
Gastroenterology; 80(5,part2):1235 1981

Transferrin was examined for its binding properties and effects on growth of a human rectal cancer cell line (HRT-18) in culture. Monolayers were cultured in multiwell plates in media containing 5% fetal bovine serum at 37 C with a 5% CO2 atmosphere and were subjected to binding studies using iodinated transferrin. Effects of transferrin on cell growth were assessed by culturing cells in serum-free synthetic medium in the presence and absence of purified human transferrin at varying concentrations for up to 14 days. Cells were able to grow satisfactorily in a serum-free synthetic medium in the absence of various hormones and growth factors. When included in a serum-free medium, transferrin stimulated cell growth. Doubling x of control cells was 3.5 days, while that of cells grown with 2ug/ml of transferrin was 1.8 days. Iodinated transferrin bound specifically to HRT-18 cells. Equilibrium of binding was attained within 20 min of incubation at 37 C and was shown to be saturable at a concentration of 40nM. Scatchard analysis of the binding data was best explained by a single linear line. The association constant (Ka) was found to be 1.3 x 108M-1 and the number of binding sites per cell was 1.8 x 10(5). In summary: 1) transferrin stimulates the growth of HRT-18 cells, and 2) transferrin specifically binds to HRT-18 cells. These data indicate that transferrin has a growth promoting effect on HRT-18 cells in culture and may affect the growth of some colonic maliignancies. (no Refs)

54. NONSPECIFIC INHIBITORY ACTIVITY OF SOLUBLE HUMAN COLON CARCINOMA EXTRACTS: TENTATIVE MECHANISM OF ACTION.

Pommier GJ, Remacle-Bonnet MM, Rance RJ, Depieds RC
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JNCI; 67(4):791-802 1981

Soluble human colon carcinoma extract(s) (SCE) were potent nonspecific inhibitors of lymphoproliferative responses to mitogens. Inhibition was concomitant with induction in about 35% of cells of morphologic alterations for most of them comparable with the ones observed in mitogen-induced blast cells. Nonetheless, these blastlike cells did not proliferate. SCE did not interfere with mitogen binding to cell receptors. Moreover, SCE was unable to induce or activate suppressor cells, and its primary target cell was the unresponsive lymphoid cell itself. The inhibitory effect of SCE was early and irreversible. The differential activity of SCE can be correlated with an early [3H]uridine uptake, which was inhibited 6 hr later, as seen for the other biochemical parameters of cell activation. Also, SCE altered membrane-bound ATPase activities. Na,K-ATPase was strongly inhibited, whereas Ca++-dependent and Mg++-dependent ATPases were stimulated. These observations were discussed as an SCE-lymphocyte plasma membrane interaction translated into differential signals to the intracellular metabolic pathways. (Author abstract) (62 Refs)

55. TRANSFORMATION ASSOCIATED FETAL ANTIGENS IN HUMAN PREMALIGNANT COLONIC EPITHELIAL CELLS (MEETING ABSTRACT).

Higgins PJ, Friedman E, Lipkin M, Hertz R, Attiyeh F
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Gastroenterology; 80(5,part2):1174 1981

Premalignant and malignant colonic cells were analyzed for transformation associated fetal antigens by immunohistologic techniques using rabbit antiserum to combined saline extracts of heart, lung, liver, kidney, spleen and small and large intestine obtained from a 2nd trimester human abortus. Antiserum had been absorbed with extracts of the corresponding adult tissues obtained at autopsy from non-cancer related deaths, and A and B RBC. Immunohistologic studies revealed anti-fetal reactivity in 84% of colonic adenocarcinomas examined by cryostat sectioning, and in all established and short term colon carcinoma cell cultures tested. Normal epithelial cells of the colon did not stain with this anti-serum. Absorption of anti-2nd trimester fetus serum with an established colon carcinoma cell line (SW 1116) removed anti-body to all tumors. Parallel absorptions with extracts of normal colonic tissues were without effect, suggesting that the anti-serum recognizes one or several closely related fetal antigens. Control experiments indicated that the antigen(s) detected was not alpha fetoprotein, beta human chorionic gonadotropin, or carcinoembryonic antigen. Primary cultures of adenomatous colonic epithelial cells were then examined for the presence of fetal antigen. Cultured epithelial cells stained positively in 2 of 11 (18%) tubular adenomas, 3 of 6 (50%) villotubular adenomas, and 5 of 6 (83%) villous adenomas. We conclude that colonic epithelial cells of human adenomas express fetal antigen with increased frequency as they progress through stages t owards frank carcinoma. (no Refs)

56. RELATIONSHIP OF SERUM CEA LEVELS TO TUMOUR SIZE AND CEA CONTENT IN NUDE MICE BEARING COLONIC-TUMOUR XENOGRAFTS.

Lewis JC, Keep PA
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London, England
Br J Cancer; 44(3):381-387 1981

The relationship of serum carcinoembryonic antigen (CEA) levels to tumor size and antigen content was studied in nude mice bearing well differentiated, mucinous human colonic-tumor xenografts. Blood samples were taken from normal nude mice and others bearing xenografts, whose size had been calculated from in vivo measurements; saline and KCl extracts were made of a proportion of these tumors. Sera and tissue extracts were assayed for CEA activity by double-antibody radioimmunoassay. Extracts were also made from the livers and spleens of tumor-bearing and normal nude mice. All normal sera and 78% of sera from tumor-bearing animals had CEA values less than 11.4 ng/ml. No clear correlation was found between serum CEA levels greater than 11.4 ng/ml and tumor size or wt, or between serum CEA and tumor CEA concentrations or total CEA burden. The concentration of CEA in those tumors tested varied from 1 to 22 ug/g. Our results confirm and extend the conclusions reached by others studying the significance of serum CEA levels with xenograft model systems. The complexity of factors contributing to circulating CEA is discussed in the light of our findings. (Author abstract) (39 Refs)

57. RELEASE OF CEA FROM HUMAN COLONIC CARCINOMAS GRAFTED INTO NUDE MICE: ARE THERE NON SECRETOR TUMORS? (MEETING ABSTRACT).

von Kleist S, Fiebig HH
Institut fur Immunbiologie, Freiburg, W. Germany
Oncodev Biol Med; AbstractsBook,1:26 1981

The close correlation between the tumor stage (total tumor burden) and carcinoembryonic antigen (CEA) serum concentration has long been established in colorectal cancer patients, yet even in these carcinomas it never reaches 100%. In other tumors, eg of the breast, this relationship is much worse: Only 30-40% of N+ and 56-72% of N+, M+ patients have elevated CEA-serum levels despite the fact that their tumors are CEA positive. We postulated that nearly all carcinomatous tissues produce CEA but not all malignant cells release it equally well. In order to further prove our point, 50 nude mice were transplanted with 9 different human colon tumor fragments of initially equal size and similar histology. Serial CEA determinations in the mice demonstrated a close correlation between log tumor vol and log CEA values. Xenografts of patients with normal serum CEA levels even when distant metastases were present, yielded near normal CEA in the serum of the nude mice. This suggests that there might be, indeed, 'non-secretor' tumors, since, even in an identical environment these tumors, although growing, did not release the CEA they contain ed, as shown by immunohistology, while other CEA positive tumors did. (no Refs)

58. THE DISTRIBUTION OF PARENTERALLY ADMINISTERED ANTIBODY TO CEA IN COLO-RECTAL XENOGRAFTS (MEETING ABSTRACT).

Lewis JC, Bagshawe KD, Keep PA
Department of Medical Oncology, Charing Cross Hospital, London, W6 8RF, England
Oncodev Biol Med; AbstractsBook,1:25 1981

Autoradiography was used to identify the distribution of parenterally administered anti-carcinoembryonic antigen (CEA) in human colo-rectal tumors xenografted to nude mice. Four xenograft lines were studied: Three mucinous adenocarcinomas of various degrees of differentiation and one anaplastic tumor. Affinity purified goat antiCEA labelled with 125 Iodine was given intravenously to xenograft bearing nude mice. At various x after administration (max 7 days), autoradiograms were prepared for 5 micron tumor sections by a modified Appleton diffusible compound technique and by conventional methods. The experiments were duplicated using a nonspecific goat gamma globulin. By combining autoradiography with a PAP immunoperoxidase method of demonstrating CEA, antiCEA was found to be preferentially retained at sites of CEA positive necrotic debris and extracellular collections of CEA positive eosinophilic material within mucinous areas. Cell surface retention was not observed. At most x following administration more antibody was detected within extracellular mucin and stromal connective tissue than within the tumor cell compartment. These studies are being followed by further experiments using monoclonal antibodies to aid design of antibody-drug conjugates for tumor therapy. (no Refs)

59. MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN (MEETING ABSTRACT)

Fuks A, Krantz MJ, Laferte S
McGill Cancer Center, Montreal, Canada
Oncodev Biol Med; AbstractsBook,1:P2 1981

Monoclonal antibodies to carcinoembryonic antigen (CEA) were developed by immunization of a Balb/c mouse with HCT-8R, a CEA-producing colonic adenocarcinoma cell line, and subsequent fusion of the immune splenocyte with P3-NS1/1-Ag4-1 mouse myeloma. Supernatants of hybrid cells were screened by a binding assay using purified radiolabeled CEA. Twenty-five of the 96 initial culture wells demonstrated anti-CEA reactivity and several of these have been cloned. The fine specificities of two of these antibodies were examined using radiolabeled CEA, the cross-reactive antigen 50,000 (50K), as well as proteolytic fragments derived from these molecules. The first antibody, b18.7.7, binds at high titre to CEA and to the major fragment derived from CEA by chemical cleavage at cysteine residues, as well as to the major fragment derived by trypsin, chymotrypsin or protease V8 digestion. Furthermore, this antibody reacts equally well with 50K, and its chymotryptic and protease V8 fragments. The second antibody d2.14.1, displays the same spectrum of reactivity as b18.7.7 with CEA and its fragments but its reactivity with 50K is significantly reduced compared with that of the first antibody. We conclude that the two anti-CEA monoclonal antibodies differ in their fine specificities towards the CEA molecule. (no Refs)

60. ESTABLISHMENT OF A CELL SYSTEM FROM RAT COLONIC CARCINOMA (MEETING ABSTRACT).

Borman LS, Swartzendruber DC, Littlefield LG
Oak Ridge Associated Universities, Oak Ridge, TN, 37830
In Vitro; 17(3):258 1981

We have established two rapidly growing, near-diploid epithelial cell lines from a specimen of the rat transplantable colon carcinoma 4047 that was subjected to 5 sequential proteolytic treatments. Successful cultures were established from the cells released from the tumor after 2nd (collagenase and elastase) and 5th (collagenase) steps. Cell lines RCC-2 and RCC-5 are distinctive with respect to morphology, modal chromosome number and karyotype, growth properties and the degree of differentiation seen in the tumors they produce in rats. The data suggest that we have recovered two different cell populations that were present in the original tumor. Three cloned cell strains have been isolated from the parental cell lines. In monolayer culture, differentiated epithelial cell types are present in the colon cancer cell lines that are characteristic of rat colon carcinoma in situ and normal colon. (no Refs)

61. LOSS OF MUCOSAL SECRETORY COMPONENTS AND CHANGES IN GLYCOCONJUGATE COMPOSITION OF RAT COLONIC TUMORS (MEETING ABSTRACT).

Jacobs LR
Department of Internal Medicine, University of California, Davis, Davis, CA, 95616
Gastroenterology; 80(5,part2):1183 1981

The aim of this study was to characterize the changes in carbohydrate composition of epithelial cell membranes (ECM) and goblet cell mucus (GCM) in transitional mucosa and benign and malignant colonic neoplasms. Colonic tumors were induced in 16 rats with 16 weekly injections of dimethylhydrazine. All animals developed neoplasms within 24 wk. Fluorescein isothiocyanate (FITC) conjugated lectins were then used to stain tissue sections from normal rats and those with tumors. Control sections were incubated with 0.3 M of the binding inhibitor to confirm specificity. Binding to N-acetyl glucosamine was measured using Wheat germ agglutinin (WGA), mannose and glucose with Concanavalin A (Con A), galactose with Ricinus communis (RCA1), sialic acid with Limulus polyphemus (LPA) and fucose with Ulex europeus (UEA1). No specific changes in lectin binding could be consistently demonstrated to ECM or to transitional mucosa. The data show that GCM and its secretory elements were absent in colonic adenocarcinoma. In benign adenomas lectin staining of GCM GlcNac, Man, Glc, Gal and Fuc residues was diminished while that of NeuNAc was unchanged; the decrease in GCM appeared to be greatest in the upper crypt. Thus alterations in GCM biosynthesis appear to correlate specifically with the degree of tumor malignancy, whereas in transitional mucosa goblet cell glyconconjugates appear normal. (no Refs)

62. CHEMICAL AND X-RAY INDUCED ANTITUMOR CELL-MEDIATED CYTOTOXICITY TO RAT FETAL CELLS (MEETING ABSTRACT).

Cheng HF, Stevens RH, Cole DA
Radiation Research Laboratory, Department of Radiology, University of Iowa, Iowa City, IA, 52242
Oncodev Biol Med; AbstractsBook,1:P20 1981

Our recent studies have indicated the presence of a common oncofetal protein (OFP) occurring in rat tumors induced in the (i) small bowel by x-rays, (ii) colon by 1,2-dimethylhydrazine, and (iii) pancreas by 7,12-dimethylbenz[a]anthracene. Measurements of the antitumor cell-mediated immune (CMI) responses of these tumor-bearing rats revealed that the peripheral blood lymphoid-cells (PBLC) expressed cytotoxicity only to entodermal tissue derived tumor target cells and not to target cells from mesodermal or ectodermal tumors. The present series of studies were carried out to determine whether such PBLC would express cytotoxicity towards normal fetal targets, thus suggesting fetal components play a role in the education of the PBLC. CMI was determined by the release of peripheral and integral radioiodinated membrane proteins of primary fetal cells derived at stage of 16-18 day gestation from the intestine, skin and whole fetus. Positive CMI was observed for PBLC obtained from the rats having the small bowel, colon, and pancreas tumors expressed to the intestine and whole fetus. While these results do not unequivocally establish an immune role for the OFP they suggest there must be some common feature of the fetal cells with that of the tumor. (no Refs)

63. QUANTITATION OF A MUTAGENIC METABOLITE PRODUCED FROM 1,2-DIMETHYLHYDRAZINE DURING LIPID INFLUENCED COLON CANCER DEVELOPMENT BY A BACILLUS SUBTILIS ASSAY.

Wargovich MJ
Texas Tech University, Lubbock, TX, 79409
Diss Abstr Int [B]; 42(4):1330-B 1981

The positive correlation between intake of dietary fat and cancer of the colon is well documented. Studies were conducted using an experimental colon carcinogenesis model to determine the role of dietary fat in the metabolism of the colon carcinogen, 1,2-Dimethylhydrazine (DMH). Bacillus subtilis TKJ6321 was used to quantify fecal mutagen and postmitochondrial enzyme in the liver and the colon mucosa of rats fed diets variable in lipid content and treated ip with DMH. Corn oil or coconut oil were used as the source of lipid for the diets. During a 32 wk schedule rats were sacrificed and autopsied for evidence of adenocarcinoma of the colon. Fecal samples were extracted and assayed for mutagenic activity by B subtilis TKJ6321 as the microbial detector of mutagenicity. Rats fed corn oil in the diet and treated wi th DMH produced a significantly higher number of adenocarcinomas of the colon. When the lipid content of the diet was raised to 10% (wt/wt) corn oil markedly stimulated enzyme induction in animals receiving DMH treatment. This induction was especially pronounced in the mutagen-producing enzyme activity of the colonic mucosa. Treatment of rats with DMH induces enzyme in the liver and colon relevant for the conversion of this compound to a mutagenic species. The extent of enzyme activity is influenced by the type of lipid supplementing the diet as is subsequent colon tumor development. (no Refs)

64. EFFECT OF INHIBITORS OF TUMORIGENESIS ON THE FORMATION OF O6-METHYLGUANINE IN THE COLON OF 1,2-DIMETHYLHYDRAZINE-TREATED RATS.

Bull AW, Burd AD, Nigro ND
Wayne State Univ. Sch. Medicine, Detroit, MI, 48201
Cancer Res; 41(12):4938-4941 1981

The level of O6-methylguanine (O6MeGua) in the colonic DNA of rats treated with 1,2-dimethylhydrazine was determined. The effect of various tumorigenesis inhibitors on the formation of this modified base was also studied. Rats were given a single sc injection of 1,2-[14C]dimethylhydrazine. Six hours later, they were killed, and colonic DNA was extracted and analyzed by high-pressure liquid chromatography. The inhibitors tested were disulfiram (DSF), pyrazole, sodium selenite, butylated hydroxyanisole, butylated hydroxytoluene, potassium ascorbate, and 13-cis-retinoic acid. The level of O6MeGua in control rats was 29.9 [(O6MeGua x 10(6)/guanine)]. When rats were fed 0.25% (w/w) DSF, this value was reduced to 10.2, and at 0.5% DSF there was not detectable O6MeGua formed. Injection of pyrazole (40 mg/kg ip) 2 hr prior to 1,2-dimethylhydrazine treatment reduced the O6MeGua level to 2.4. All the other tumorigenesis inhibitors had no effect on either O6MeGua levels or the cpm/mg DNA in treated rats. With O6MeGua as a measure of the extent of initiation, these results confirm that DSF and pyrazole inhibit the initiation phase of carcinogenesis. This is to be expected as both have been shown to block the metabolism of azoxymethane, which is a crucial metabolite in the activation of 1,2-dimethylhydrazine. The other substances, all known tumorigenesis inhibitors, may act on the promotional phase of carcinogenesis and are worthy of further study for their role in cancer prevention. (Author abstract) (22 Refs)

65. EFFECT OF ANTIBIOTICS ON INCIDENCE OF RAT INTESTINAL TUMORS INDUCED BY 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE.

Goldin BR, Gorbach SL
Infectious Disease Service, Dept. Medicine, New England Medical Center Hosp., Tufts Univ. Sch. Medicine, 171 Harrison Ave., Boston, MA, 02111
JNCI; 67(4):877-880 1981

The intestinal microflora has been shown to influence the induction of chemical carcinogens responsible for intestinal tumors in animal models. For further exploration of this issue, male inbred F344 rats were administered a chemical carcinogen, 1,2-dimethylhydrazine dihydrochloride (DMH), for 20 wk, along with oral antibiotics, either tetracycline or erythromycin, to suppress the intestinal flora. Colon cancer incidence was lower in animals receiving antibiotics; 22% of the erythromycin-treated rats and 20% of the tetracycline-treated rats had colon tumors compared to untreated controls with a 74% tumor incidence (p less than 0.002). Tumors in the small intestine also decreased from an incidence of 48% in the control animals to an incidence of 27 and 7%, respectively, for the erythromycin- and tetracycline-treated rats. These findings suggested that the metabolic activity of the intestinal flora is related to cancer induction by DMH. (Author abstract) (23 Refs)

66. ADENOCARCINOMA IN URINARY DIVERSION TO THE COLON: EXPERIMENTAL STUDIES (MEETING ABSTRACT).

Gittes RF, Crissey M
Peter Bent Brigham Hospital, Boston, MA
Br J Urol; 53(1):72 1981

Adenocarcinoma of the colon arising at the junction of the urinary and colonic epithelia occurs in over 5% of patients with long-term ureterosigmoidostomy. A model of this localized tumor has been achieved in rats, such tumor arising in 12 of 17 rats surviving 8 to 12 mo after diversion of the urinary bladder to empty into the rectum. The question of whether such tumors might arise clinically in colon loops was addressed also. Rats with a colostomy diverting the fecal stream proximal to their urinary-colonic junction never developed junctional tumors (0/31). It is apparent that isolated intestinal conduits are not especially susceptible to urine-born carcinogens, but that the admixture of feces and urine somehow activates carcinogens which are short-lived and act upon the junctional intestinal epithelium. The model offers the opportunity for experimental definition of this condition and perhaps prevention of this localized form of tumor. (no Refs)

67. PARTIAL COLECTOMY PROMOTES EXPERIMENTAL CARCINOGENESIS ONLY AT THE SITE OF INTESTINAL ANASTOMOSIS (MEETING ABSTRACT).

Williamson RC, Davies PW, Bristol JB, Wells M
University Department of Surgery, Royal Infirmary, Bristol, England
Gut; 22(5):A440 1981

The possibility that metachronous colorectal cancers arise in mucosa rendered hyperplastic by partial intestinal resection was tested in male Sprague-Dawley rats weighing 159 +/-14 g (standard deviation). Rats received mid-colonic transection, right or left hemicolectomy, cecal resection, or no operation (controls). Each operation was performed either before or one wk after a course of five weekly sc injections of azoxymethane (10 mg/kg/wk) or water. The timing of operation did not affect ultimate tumor yields. Although cecal resection and right hemicolectomy both increased ileal wet wt by 22-40%, there was no evidence of adaptive growth in the colon after partial colectomy. A total of 217 large-bowel tumors were distributed as follows: proximal colon 16.5%, colonic anastomosis 23.5%, distal colon 40%, rectum 20%. Consistent with this leftsided predominance, left hemicolectomy reduced the number of tumors by 52-58% compared with transection or controls. Cecal resection had no effect. A twofold increase in distal tumors after transection and right hemicolectomy reflected the many anastomotic tumors found after each operation. Moreover, one rat receiving vehicle (not carcinogen) developed an invasive mucinous adenocarcinoma at the colorectal anastomosis after left hemicolectomy. Ileocolic and colorectal anastomoses are favored sites for tumor development after partial colectomy. The lack of adaptive hyperplasia may explain unaltered carcinogenesis in the remaining colon. (no Refs)

68. FAILURE OF DIETARY CELLULOSE FIBER TO PREVENT COLON TUMORS IN DIMETHYLHYDRAZINE (DMH)-TREATED RATS ON HIGH CHOLESTEROL DIETS (MEETING ABSTRACT).

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Department of Internal Medicine, Veterans Administration Medical Center, Omaha, NE, 68105

Gastroenterology; 80(5,part2):1301 1981

A prior study has suggested that dietary fiber (cellulose) may decrease colon carcinogenesis in the DMH-induced rat model. We have evaluated the effect of dietary cellulose fiber on DMH-induced colon tumors in rats fed high cholesterol diets (a suspected co-carcinogen with DMH). Synthetic diets containing excess cholesterol and variable fiber content were fed to male Sprague-Dawley rats: Group I (0% fiber), Group II (5% fiber), and Group III (20% fiber). Half of each group received sc injections of DMH for 20 wk. Control rats received saline. All animals were sacrificed 1 wk after the last injection and blood obtained for cholesterol determination. Rat colons were inspected grossly and microscopically for invasive adenocarcinoma. Saline control animals were tumor free. No difference in either tumor incidence or number of tumors per affected rat colon was observed. Furthermore, the presence of dietary fiber did not alter serum cholesterol level supporting prior observations that cellulose fiber does not affect cholesterol metabolism. These findings suggest excess dietary cholesterol may diminish the protective effect of dietary fiber on DMH-induced colon tumors, possibly through an intraluminal mechanism. (1 Ref)

69. HIGH DIETARY CELLULOSE: PROTECTION AGAINST LARGE BOWEL CARCINOMA (MEETING ABSTRACT).

Prizont R, Platt K

Division of Gastroenterology, Albuquerque Veterans Administration Medical Center, Albuquerque, NM

Gastroenterology; 80(5,part2):1256 1981

The effect of high cellulose diet in experimental carcinogenesis, was investigated in Wistar rats injected ip with 10 doses of 1,2 dimethylhydrazine (DMH). Ten experimental animals (ER) were fed a regular diet of casein (20%), sucrose (50%), fat (5%) and cellulose fiber (5%). A second group (EHF) received a similar diet modified by an increase of cellulose (to 15%) and a concomitant 10% decrease of sucrose. Two groups of 6 rats each were injected with buffer and used as animal controls on a regular or high fiber diet. When food consumption was measured, ER animals averaged 20.5 +/-0.3 g/day and EHF rats, 22.7 +/-0.3 g/day. In the same period of time, ER animals had significantly (p less than 0.005) lower fecal outputs than did EHF rats. Rats were sacrificed 7 mo after initial DMH injection. Conversely, 17 intestinal tumors were found in ER animals, which was significantly higher than the 4 recovered from EHF rats. Histological examination revealed that 15 of the 17 ER tumors were malignant (14 adenocarcinomas and 1 signet ring carcinoma). Only 2 of the EHF tumors were adenocarcinomas. The small intestine of ER rats contained 9 tumors (8 adenocarcinomas). The same area in EHF animals yielded 4 tumors (2 malignant). The large intestine of ER rats contained 8 neoplasms (7 malignant), but no benign or malignant tumors were found in the EHF large bowels. This study indicates that DMH injected rats fed a high cellulose diet develop significantly fewer intestine tumors. (1 Ref)

70. MECHANISM OF FIBRE PROPHYLAXIS OF CHEMICALLY INDUCED COLONIC CARCINOMA IN THE RAT (MEETING ABSTRACT).

Harvey JS

Department of Surgery, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, England

Eur Surg Res; 13(1):96 1981

The prophylactic effect of fiber on colonic carcinogenesis may be due to a reduction in energy intake rather than an effect on stool bulk and transit time. To test this hypothesis colon cancer was induced in rats whose diet was varied for energy intake as well as fiber intake. Sixty-two weanling rats were divided into four groups, matched for wt and rate of growth. All animals were given sc injections of dimethylhydrazine dihydrochloride (20 mg/kg at 10-day intervals for 150 days). The animals were housed and fed as follows until sacrificed at 170 days; group 1: normal diet ad lib, caged in fours; group 2: high fiber diet ad lib, caged in fours; group 3: high fiber diet ad lib, caged singly; group 4: normal diet restricted to the same energy, intake as group 3, caged singly. Adult mean wt with cancer incidences (in parentheses) were: group 1: 421 g (14/16); group 2: 391 g (14/16); group 3: 369 g (8/15); group 4: 358 g (10/15). There were no significant differences in cancer incidences between any of the groups taken individually and simply feeding fiber was not seen to offer any protection. Groups 1 and 2 combined had a significantly higher incidence of cancer than the smaller animals in groups 3 and 4 combined, which favors the hypothesis that any effect that fiber may have is related to cal restriction rather than to its mechanical effects in the bowel. (no Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

71. FAMILIAL INCIDENCE OF COLORECTAL CANCER (MEETING ABSTRACT).

Duncan JL, Kyle J

Gastrointestinal Research Unit, Royal Infirmary, Aberdeen, Scotland

Gut; 22(5):A435 1981

A prospective study of the familial incidence of cancer has been performed on 50 consecutive patients treated for adenocarcinoma of the colon and rectum. All diagnoses were confirmed histologically and the presence or absence of adjacent polyps was noted. Each patient was questioned about all first-degree relatives, particularly in regard to intestinal cancer. Confirmation was obtained from pathology reports or close relatives. The control group consisted of 50 patients, matched for age and sex, and who did not have cancer. Nine out of the 50 patients had a parent, sibling, or child with colorectal cancer (18%). In five out of the nine families the mother was the other affected member. In the control group only two patients had an affected relative (4%). The difference is highly significant. The familial incidence was, comparable with the 16% incidence noted in Nebraska, but the 'cancer families' with more than two affected members were not encountered in the present series. There was no difference in the frequency of polyps in the group of patients who had affected relatives (22%) compared with the group whose close relatives to date are free from colorectal cancer (24%). The implications for screening programs are discussed. (no Refs)

72. EARLY IDENTIFICATION OF INDIVIDUALS AT INCREASED RISK FOR CANCER OF THE LARGE INTESTINE. PART II: DEVELOPMENT OF RISK FACTOR PROFILES.

Lipkin M, Winawer SJ, Sherlock P
Gastroenterology Service, Dept. Medicine, Memorial Sloan-Kettering Inst., New York, NY
Clin Bull; 11(2):66-74 1981

Studies to determine indices or markers identifying persons with inherited susceptibility to colorectal cancer are described. A discussion is presented of biological characteristics associated with genetic predisposition to large bowel cancer, not only during growth of benign and malignant neoplasms but also before the appearance of clinically detectable lesions. Modified epithelial cell proliferative activity may indicate predisposition. During progressive stages of abnormal development, epithelial cells gain increased ability to proliferate and accumulate in the mucosa. In subjects with familial polyposis, patches of flat mucosa are found which have colonic epithelial cells that fail to repress DNA synthesis during migration to the surface. The change occurs in normal-appearing colonic epithelial cells before and after the cells undergo adenomatous change and begin to accumulate as polyps. Observed in greater than 80% of random biopsy specimens, the failure to repress DNA synthesis has been shown to occur both in patients with polyposis coli and in certain cancer-prone families. Other early markers for increased risk of colorectal cancer are discussed. (44 Refs)

73. RECTOCOLIC FAMILIAL POLYPOSIS; A STUDY OF 32 CASES.

Bigay D, Plauchu H, Berard P, Robert JM, Guillemin G
(c/o Guillemin) Clinique chirurgicale C, Hotal Dieu, Place de l'Hopital, 69288 Lyon Cedex 1, France
World J Surg; 5(4):617-625 1981

Thirty-two cases of diffuse rectocolic polyposis are analyzed with respect to diagnosis, pathologic features, familial and genetic factors, surgical treatment, and relationship to development of colorectal cancer. Homogeneity of the series allows precise observations to be made on evolution and treatment of the disease. Fourteen of the 32 patients developed malignancies, most occurring in the rectum and sigmoid. Rectal resection is recommended in cases of endoscopically demonstrated local degeneration or advanced disease. (24 Refs)

74. CANCER IN ULCERATIVE COLITIS: GOOD NEWS AND BAD NEWS.

Sachar DB, Greenstein AJ
Mount Sinai Medical Center, New York, NY
Ann Intern Med; 95(5):642-644 1981

Estimation of the true incidence of colorectal cancer in ulcerative colitis is discussed, with an emphasis on the role of ascertainment bias in substantial overestimate of risk. Long-term survival in patients with colitis-associated cancer has been shown to be no worse than that in patients with de-novo colorectal cancer. Patients with severe dysplasia should undergo colectomy. (21 Refs)

75. A NEW LOOK AT THE CANCER RISK IN ULCERATIVE COLITIS (MEETING ABSTRACT).

Gyde S, Prior P, Waterhouse JA, Allan RN
Gastroenterology Unit, The General Hospital, Birmingham, England
Gut; 22(5):A418 1981

The magnitude and pattern of risk of colorectal cancer in ulcerative colitis is uncertain, the apparent risk varying greatly from one reported series to another. In this analysis several models have been used to show how selection factors, operating in most reported series, may alter the apparent cancer risk and the pattern of risk over time. These models have been applied to a hospital series of 676 patients under long-term review with ulcerative colitis. The number of colorectal and hepatobiliary cancers observed in the series was significantly in excess of that expected in a comparable general population. The colorectal cancer risk varied from six to 17 x that in the general population according to which model was used for analysis. This variation helps to explain the widely differing estimates of colorectal cancers in published series. The model which seems to most closely resemble the natural history of the disease suggests that the risk of developing colorectal cancer increases in the first 15 yr after onset of ulcerative colitis and thereafter becomes a constant increased risk. This pattern suggests that cancer may be initiated and colitis induced by a common etiological agent at or near the onset of colitic symptoms. (no Refs)

76. GALLBLADDER DISEASE: RISK FACTOR FOR COLORECTAL CARCINOMA? (MEETING ABSTRACT).

Allende HD, Ona FV
Department of Medicine, University of Rochester, Rochester, NY
Gastroenterology; 80(5,part2):1099 1981

A study of the relationship between the state of the gallbladder and the risk of colorectal carcinoma is reported. Eight hundred and sixty-four consecutive adult postmortem examinations were reviewed. Data recorded and analyzed were: 1) sex, 2) presence or absence of colorectal cancer, 3) state of the gallbladder, in this study classified as: a) normal, b) cholelithiasis, c) surgically absent. Statistical analysis was carried out by max likelihood and standard Chi-square methods. Gallbladder disease was defined as either cholelithiasis or cholecystectomy. The analysis confirmed the known association between the female sex and gallbladder disease and revealed that after correcting for this association the prevalence of colorectal cancer was higher among cholelithiasis and cholecystectomy cases. The frequency was higher among cholecystectomy than among cholelithiasis cases but this difference was not statistically significant. Previous studies of the possible association between cholecystectomy and colorectal carcinoma have been contradictory, probably because they failed to evaluate the entire spectrum of gallbladder state from health to max disease. It is concluded that the state of the gallbladder modifies the risk of colorectal carcinoma. (no Refs)

77. INCREASED RISK OF COLORECTAL CANCER AFTER CHOLECYSTECTOMY.

Turunen MJ, Kivilaakso EO
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Ann Surg; 194(5):639-641 1981

The relative risk of developing colorectal cancer after cholecystectomy has been assessed in a retrospective autopsy study using controls individually matched for age and sex. Of the 304 patients dying with colorectal cancer and undergoing autopsy examination at the Helsinki University Central Hospital, 45 had undergone previous cholecystectomy. The corresponding number for the matched-pair controls without colorectal cancer was 32, indicating that the relative risk of developing colorectal cancer is slightly (1.59), but significantly (p less than 0.05), increased after cholecystectomy. The relative risk was highest for cancer of the right colon (3.00). In contrast, no difference in the autopsy incidence of unoperated gallstones was observed between the two groups, suggesting that, rather than lithogenic bile alone, the predisposing factor is related to the cholecystectomy procedure itself. (Author abstract) (17 Refs)

78. RELATIONSHIP BETWEEN CHOLECYSTECTOMY AND COLORECTAL CANCER (MEETING ABSTRACT).

Caprilli R, Pietroiusti A, Chierchini P, Giuliano M, Andreoli A, Prantera C
Unita Gastroenterologica II Clinica Medica, Universita di Roma, Rome, Italy
Gastroenterology; 80(5,part2):1120 1981

The records of 773 patients admitted for colorectal cancer to two Rome hospitals during a ten-yr period were retrospectively examined. Diagnosis had been confirmed histologically in all cases. A sex and age matched control admitted to the same hospital during the same calendar period was selected for each case. Fisher's test was used for the analysis of data. Thirty-five (4.5%) patients with carcinoma of the colon and forty-seven (6%) controls had been submitted, 2-31 yr previously, to cholecystectomy but no significant difference was found between the two groups. The difference remained unchanged even when patients with a history of conditions at risk for cholelithiasis were excluded from both groups. Furthermore, the two groups were comparable with respect to longstanding cholecystectomies (more than five yr). The distribution of cancer by subsite was similar in cholecystectomized and non cholecystectomized patients. No gradient of previous cholecystectomy from ascending colon cancer to rectal cancer was found, as reported by others. In conclusion, the results of this study do not indicate that cholecystectomy may be regarded as a risk factor for the development of large bowel cancer and in particular right-sided carcinoma. (no Refs)

79. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A
Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada
Soc Sci Med [Med Geogr]; 15(1):213-223 1981

Epidemiologic studies of the carcinogenicity of drinking water are reviewed, and results of an investigation of the relationship between the quality of drinking water and cancer in Quebec are presented. Standardized incidence ratios (SIRs) for gastrointestinal, urogenital and other neoplasms (1971-1975) were calculated for 46 Quebec census regions in which at least 50% of the population was supplied with drinking water from the St Lawrence river. Regions with high and low SIRs were compared according to the physicochemical characteristics of the drinking water. Correlation and regression analysis revealed a significant positive association between 'soft' water and the incidence of cancer of prostate, rectum, and digestive system organs. 'Hard' water was negatively associated with the incidence of stomach, prostate, and rectal cancer. (46 Refs)

80. FACTORS ASSOCIATED WITH ADENOCARCINOMAS OF THE LARGE BOWEL IN PUERTO RICO.

Martinez I, Torres R, Frias Z, Colon JR, Fernandez N
Cancer Control Program, Dept. Health, Puerto Rico
Rev Latinoam Oncol Clin; 13(1):13-20 1981

A case-control study of 461 patients with adenocarcinoma of the colon seen durin g the period 1973-1975 and 461 sex- and age-matched controls was conducted. Subjects or relatives (102 pairs) were questioned on long-term dietary and personal habits, and familial aggregation of cancer. Of the 461 adenocarcinomas, 232 were in the colon and 229 were in the rectum and rectosigmoid junction (1.2:1 male-female ratio). Highest number of patients were 65-74 yr old. Twenty-two percent of patients were professionals vs 18.5% of controls. Significantly more patients (29.1%) than controls (16.5%) were heavy cigarette smokers. Patients reported significantly greater frequency of consumption of meats (34.7% high frequency vs 24.3% in controls), cereals (26.7% vs 18.7%), fats (49.2% vs 36.7%), total residue (36.4% vs 29.5%), and fiber (51.4% vs 42.3%). Patients also had more previous nonmalignant chronic disease of the large bowel (diverticulosis, intestinal polyposis, ulcerative colitis, other types of colitis, chronic constipation, diarrhea, and hemorrhoids), higher grade of constipation, and more direct relatives with cancer (for cancer of the large bowel, 22 relatives among patients vs 9 among controls). Recall bias may be expected in this type of study. (25 Refs)

81. LARGE BOWEL CANCER IN AUCKLAND, NEW ZEALAND 1965-1975.

Alley PG
Dept. Surgery, Sch. Medicine, Univ. Auckland, Auckland, New Zealand
NZ Med J; 94(690):131-133 1981

Between 1965 and 1975, 2,684 cases (1,267 men; 1,417 women) of colorectal cancer were reported in Auckland. Of these, 1,726 cases (758 men; 968 women) had colon cancer and 958 (509 men; 449 women) rectal cancer. Resection of the primary lesion was done in 84.9% of those with colon cancer and in 88.6% of those with rectal cancer. The av age of presentation for men with colon cancer was 61 yr, for women it was 69 yr. The av age of presentation for rectal cancer was equal for both sexes at 69 yr. Survival was poor for cancer of the proximal colon but increased to a corrected 5-yr survival of 44.5% in the rectum. Overall 5-yr survival was 41.9%. For patients whose primary lesion was resected from the colon the corrected 5-yr survival was 45%. For patients with rectal cancer it was 48.6%. The mean survival time for patients treated by resection was 28.5 mo for colonic lesions and 29.8 mo for rectal lesions. Where the primary lesion was not excised mean survival was less than 5 mo. This study shows that New Zealand has one of the highest age standardized incidences of colorectal cancer for European men and women, and that despite an aggressive surgical approach the survival remains low, presumably because of occult metastases present at the time of initial treatment. (10 Refs)

82. ASSESSMENT OF THE ROLE OF MUTAGENS AND ENDOGENOUS FACTORS IN LARGE BOWEL CANCER.

Weisburger JH, Spingarn NE, Wang YY, Vuolo LL
American Health Foundation, Valhalla, NY
Cancer Bull; 33(4):124-129 1981

Etiology of large bowel cancer is discussed. The production of abnormal DNA through the direct attack of radiation, chemicals, or viruses, or through improper DNA polymerase activity during DNA synthesis or repair, is only the first step in a long sequence of events terminating in a malignant invasive neoplasm. Rate of cell duplication as controlled by promoters or inhibitors is also important for neoplasm development. Chemical carcinogens, accounting for the majority of human cancers, can be divided into two major groups: genotoxic (direct-acting, procarcinogen, and inorganic carcinogen) and epigenetic (solid-state carcinogen, hormone, immunosuppressor, co-carcinogen, and promoter). Colon cancer incidence and mortality vary as a function of geographic area of residence. The key environmental difference between low-risk and high-risk countries appears related to diet, particulary fat and fiber consumption. In order for colon cancer to occur, both promoters (ie high fat diet) and initiators (ie mutagens produced during frying or broiling of meats and fish) may be required. Variations in these factors and high fiber intake can alter the incidence of colon cancer. (38 Refs)

83. CANCER OF THE COLON.

Audigier JC, Lambert R
Faculte de medecine, Centre d'Epidemiologie du CNRS LP005440, avenue Rockefeller, 69373 Lyon Cedex 2, France
Gaz Med Fr; 88(28):3903-3909 1981

Epidemiological factors related to colon cancer (CC) are considered. The number of CC cases increases linearly with age for both sexes. The male:female CC ratio is usually greater than 1. The genetic factor is most evident in CC developing in patients with multiple polyposis or extracolonic tumors (Gardner's syndrome). Geographic variations in the incidence of CC are described. Through the study of persons migrating from Japan or Poland to the United States, a country at high risk for CC, the importance of environment and diet in the development of CC is evident. Variations in CC incidence over time are discussed. The risk of CC is greater in persons with polyps. The malignant potential of these adenomas varies according to the size, histological type, and degree of epithelial abnormality of the lesions. Adenomatous polyps are usually small and less likely to become malignant than are villous polyps. Patients with inflammatory intestinal disease, such as ulcerative colitis and Crohn's disease are more likely to develope CC. An excess of animal fats and cholesterol and a lack of fiber are the dietary factors most often related to the development of CC. The early detection and prevention of CC are discussed. (10 Refs) (In FRE)

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Diagnosis, Treatment

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. CT APPEARANCE OF THE PELVIS AFTER ABDOMINO-PERINEAL RESECTION FOR RECTAL CARCINOMA.

Lee JK, Stanley RJ, Sagel SS, Levitt RG, McClennan BL
Mallinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, 510 S. Kingshighway, St. Louis, MO, 63110
Radiology; 141(3,part1):737-741 1981

CT scans of the pelvis in 40 patients who had undergone abdomino-perineal resection for advanced rectal carcinoma 2 wk to 24 yr earlier were reviewed to determine whether there was any difference between simple postoperative change and local recurrence. Of 21 patients with no recurrence, the postoperative bed was clean in 10 and contained minimal streaky densities in 11. In contrast, a globular mass of soft-tissue density greater than or equal to 1.5 cm in diameter was noted near the operative site in 19 patients with recurrence. Factors which may contribute to the disparity between these findings and those of previous investigators are discussed. (Author abstract) (5 Refs)

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HE 20. 3173/2:

2. RECTOCOLIC LYMPH NODE APPEARANCE IN ADULTS.

Weissman A, Barge HJ, Clot M, Saigot T, Harriague D, Curet P, Grellet J
(c/o Grellet) Service Central de Radiologie, Hopital La Pitie, 83, boulevard de l'hopital, F 75013 Paris, France
J Radiol; 62(8/9):449-455 1981

A very characteristic rectocolic lymph follicle appearance was observed on radiological examination by double contrast enemas in 3.5% of 480 cases explored. The usual typical appearance is that of small lacunae of 1 to 3 mm in diameter, with indistinct borders, extending through several colon segments. The frequency with which these images are observed is probably a function of the double contrast technique employed, perticularly the adherence of the barium. In most cases, the lymph follicle appearance is a variation of the normal, but several rare forms could result from a partial immunity deficiency. Differential diagnosis includes colon wall edema and most polyposis disorders in their initial stages. Coloscopy with biopsy is necessary when diagnosis is uncertain. (Author abstract) (43 Refs) (In FRE)

3. X-RAY DIAGNOSTIC IMAGING OF SMALL ELEVATED LESIONS OF THE LARGE INTESTINE.

Matsuura K, Kitagawa S
Dept. Radiology, Kyushu Univ. Sch. Medicine, Kyushu, Japan
Nippon Rinsho; 39(5):99-106 1981

Large intestinal x-ray features were examined in 2,093 patients who underwent barium x-rays from 1974-1980. Polyps were diagnosed in 514 patients, cancer in 170 (32 early stage), and localized lesions in 719. Polyps were classified into three groups: Group A polyps were those with positive x-ray and endoscopic findings, Group B polyps were those with positive x-ray findings and negative endoscopic findings, and Group C polyps were those with negative x-ray and endoscopic findings. Of all the polyps, 65% were Group A, 19% Group B, and 16% Group C. Of polyps less than 5 mm, 52% were Group A, 26% Group B, and 22% Group C. Polyps less than 5mm were found associated with cancer and diverticulitis in 10/34 Group C and 9/40 Group B patients. In cases of oral-side intestinal constriction accompanying cancer, colitis, and hyperextended transverse colon, a gyroscope was used to implement the flow of 50% w/v barium. This procedure allowed good visualization of the lesions that were impossible to view with endoscopy or double contrast roentgenography utilizing 60-70 % w/v barium. (12 Refs) (In JPN)

4. 99MTC RED BLOOD CELLS FOR DETECTION OF GASTROINTESTINAL BLEEDING: EXPERIENCE WITH 80 PATIENTS.

McKusick KA, Froelich J, Callahan RJ, Winzelberg GG, Strauss HW
Nuclear Medicine Div., Massachusetts General Hosp., Boston, MA, 02114
AJR; 137(6):1113-1118 1981

Imaging was done in 80 patients with gastrointestinal hemorrhage using red blood cells labeled with 99mTc by a modified in vivo technique. Bleeding was detected in 65% of 40 patients with bright red blood per rectum, 71% of 35 patients with melena, and in none of the five patients with occult bleeding and chronic anemia. No clinical evidence of further gastrointestinal hemorrhage occurred in 26 of the 29 patients who were negative on imaging. The imaging study could be carried out for over 24 hr which increased the sensitivity of the test, since only 16% of the studies were abnormal on the initial images. Neither the need for blood replacement nor the presence of bright red blood per rectum correlated strongly with early image positivity, supporting the contention that patients with gastrointestinal hemorrhage do not necessarily bleed continuously. Labeled red cell imaging was more sensitive in the detection of bleeding than angiography. It corresponded to the overall angiographic findings in 23 of 31 cases and in 17 of the 18 patients who had demonstrable extravasation. 99mTc red blood cells may be used effectively in patients with melena as well as with bright red blood per rectum, and thus would seem to be the preferred radiopharmaceutical for imaging. (Author abstract) (8 Refs)

5. EARLY DIAGNOSIS OF METACHRONOUS COLORECTAL CARCINOMA.

Tornqvist A, Ekelund G, Leandoer L
(c/o Ekelund) Dept. Surgery, Univ. Lund, Malmo General Hosp., S-214 01 Malmo, Sweden
Aust NZ J Surg; 51(5):442-445 1981

The frequency of metachronous colorectal tumors in a prospective 20-yr series of patients with colorectal cancer is reported. Thirty-one patients, that is 2.1% of the patients operated on for cure, had metachronous carcinomas, and 5.4% had metachronous polyps. One-third of the metachronous carcinomas were diagnosed at scheduled postoperative control examinations, and the others because of their symptoms or at autopsy. The reported metachronous carcinomas are considered to represent failures of follow-up only and not to indicate their true incidence, since their natural course has been arrested by removal of adenomas whenever found. Several of the metachronous tumors were judged to be overlooked synchronous ones, and therefore a thorough postoperative examination of the remaining large bowel is advocated. The finding of subsequent tumors in this series indicates that continuous follow-up is worthwhile. (Author abstract) (9 Refs)

6. BIOPSY DIAGNOSIS WITH ENDOSCOPIC POLYPECTOMY.

Tomizawa M, Nomoto M
Third Dept. Internal Medicine, Niigata Univ. Sch. Medicine, Niigata, Japan
Nippon Rinsho; 39(5):95-98 1981

Results of large intestinal polypectomy biopsies performed in 136 patients (85 men, 51 women) were discussed. Approx 10% of the biopsy specimens were limited to the mucosa; these were pedunculated or non-pedunculated adenocarcinomas within adenomas. Approx 5% were submucosal cancers, 0.8-2.7 cm large, and were either non-pedunculated flat or semi-pedunculated. Adenomatous polyps were observed most frequently and 82% of these were adenocarcinoma within adenomas. Histological types of these adenomas were tubular adenoma (91%), tubulovillous adenoma (8%), and villous adenoma (1%). Other types of lesions that were observed among the biopsy specimens were juvenile polyps and Peutz-Jeghers type tumors. Sometimes special procedures need to be used to preserve the biopsy specimen during recovery; tubes may be inserted past the sigmoid flexure to insure that the specimen is not damaged when pulled through that area or the anal sphincter. Histological examination of the central portion of the polyp with the aid of thin layer sectioning was recommended. Preservation of the remainder of the specimen was recommended to allow definitive diagnosis of cancer when cancer foci might exist in areas other than in the central portion of the specimen. Examination of the specimen for carcinomatous invasion of the submucosa and vascular tissue was also thought to be important for diagnosis of the extent of cancer. (11 Refs) (In JPN)

7. CANCER OF THE LARGE INTESTINE AND INVASION OF VESSELS.

Aso K, Takahashi T, Igarashi M
Dept. Surgery, Kitasato Univ. Sch. Medicine, Sagamihara, Japan
Nippon Rinsho; 39(5):162-167 1981

Cancerous invasion of blood and lymphatic vessels was investigated in 155 patients who underwent surgery for cancer of the large intestine. Surgical specimens were examined with hematoxyline-eosine and elastica van Gieson stains. Degrees of lymphatic vessel invasion (ly0-3) and venous invasion (v0-3) were significantly (p less than 0.001) correlated in 68 patients with rectal cancer, and 87 with colon cancer. Patients with invasion of the intestinal vessels often showed high degrees of cancerous invasion. Invasion of vessels at the periphery of the primary tumor and at the submucosal and subserosal levels of the intestine were observed often; depth of tumor infiltration and degree of vessel invasion were correlated. Classification of the tumors by macroscopic type indicated that types of tumors that had strong trends of infiltration included many cases in which vessel invasion was observed. The INF classification system was significantly (p less than 0.05) correlated with vessel invasion. The Astler and Coller classification system was significantly (p less than 0.05) correlated with lymphatic vessel invasion. All of the patients who had hepatic metastasis were classified as ly3 and v3, indicating a high degree of invasion. (13 Refs) (In JPN)

8. EVALUATION OF THE TNM CLASSIFICATION SYSTEM FOR CANCERS OF THE COLON AND RECTUM AND PROPOSAL FOR ITS REVISION.

Yasutomi M, Takahashi T, Kato K, Muto T, Yoshio T, Koyama T
Dept. Surgery, Kinki Univ. Sch. Medicine, 380, Nishiyama, Sayama-cho, Minami Kawachi-gun Osaka 589, Japan
Jpn J Clin Oncol; 11(2):335-342 1981

An assessment of the new tumor, node, and metastases (TNM) classification of colorectal tumors based on experience in Japan is presented, and revisions suggested. One problem with the TNM classification is the difficulty in distinguishing pT categories accurately. The distinction between contiguous structures and adjacent organs or tissues becomes difficult because the same pT classification is applied to both the serosa-covered colon or upper rectum and the non-serosa-covered lower rectum. While a tumor with extension beyond the proper muscle layer involving the serosa is classified as pT2 in the case of serosa-covered colon and the upper rectum, in the not serosa part of the rectum even a tumor with minimal extension into contiguous tissues is classified as pT3, in spite of the same or lesser grade of penetration. Definitions of pT3 and pT4 as applied to colorectal cancer are not applied to cancer of the stomach, even though both are digestive tract tumors within the peritoneal cavity. It is believed that pT3 for cancers of the colon should be included in pT4. It is thus proposed that the pT categorization for cancers of the colon and rectum should follow the pT categorization for cancer of the stomach, in which pT2 applies to cancer invading the muscularis, pT3 to that penetrating beyond the muscle with or without invasion to the serosa, and pT4 to that penetrating to the contiguous structures and/or adjacent organs. (4 Refs)

9. HISTOLOGICAL TYPE OF LARGE INTESTINE CANCER AND ITS PROGNOSIS.

Hirota T, Okada T, Itahashi M, Moriya N, Koyama Y, Hojo K
First. Histopathological Res. Room, Natl. Cancer Center Res. Inst., Chuo-ku, Tokyo 104, Japan
Nippon Rinsho; 39(5):112-120 1981

Relationship between histological type and prognosis was examined in 657 cases (361 men, 296 women) of curatively resected cancer of the large intestine. Histologically, 508/657 tumors were well-differentiated adenocarcinoma, 67 were moderately differentiated adenocarcinoma, 17 were poorly differentiated adenocarcinoma, 56 were mucinous carcinoma (MC) and 9 were other types. According to Dukes' classification system, 110 were Dukes' A, 261 were Dukes' B, and 286 were Dukes' C. Overall, the 5-and 10-yr survival rates of the 657 patients were 65.2% and 57.6%, respectively. The 5-and 10-yr survival rates of patients according to histological types were 68.1% and 60.6%, respectively, for differentiated adenocarcinoma (575 cases) and 40.6% and 31.6%, respectively, for MC. The 5- and 10-yr survival rates of the patients with Dukes' C cancer were 43.6% and 38.2%, respectively, for those with differentiated adenocarcinoma and were 30.2% and 19.0%, respectively, for those with MC. Because of the small numbers of patients with signet-ring carcinoma, squamous cell carcinoma, adenosquamous carcinoma, and undifferentiated carcinoma, it was impossible to determine which histological type of cancer was associated with the poorest prognosis, but compared to patients with differentiated adenocarcinoma, those with MC had a poor prognosis. (13 Refs) (In JPN)

10. RATE AND PATTERN OF EPITHELIAL CELL PROLIFERATION IN ULCERATIVE COLITIS.

Serafini EP, Kirk AP, Chambers TJ
Dept. Experimental Pathology, St. Bartholomew's Hosp. Medical Coll., London, England
Gut; 22(8):648-652 1981

We investigated the pattern of proliferation of epithelial cells in rectal mucosa taken from normal individuals and patients with ulcerative colitis by incubating mucosa with tritiated thymidine in vitro and processing for autoradiography. We found that patients with ulcerative colitis in remission showed a proliferative pattern similar to that seen in both regenerating and 'precancerous' mucosa. Patients with a short history were as likely to show this pattern as those with a long history, and this shows that the abnormal pattern does not signify impending malignant change. We also found that mucosa from patients with ulcerative colitis in remission showed an increased proportion of cells synthesizing DNA, a proportion surprisingly close to that seen in an active phase; this suggests that the abnormal pattern seen in remission is the pattern of a regenerating mucosa. We feel that this high rate of mucosal turnover, sustained not just during clinically active disease but throughout remission, leads to the increased incidence of carcinoma and to the development of carcinoma in flat mucosa. (Author abstract) (12 Refs)

11. MOVEMENT OF LARGE INTESTINAL MUCOSA AND ROTATION OF LARGE INTESTINAL CANCER CELLS.

Hattori T
Pathologisches Institut der Universitat Bonn, 5300 Bonn, W. Germany
Nippon Rinsho; 39(5):36-41 1981

Cellular movement of normal large intestinal mucosa, dynamics of growth of adenomas in the large intestine, and the dynamics of proliferation of large intestinal carcinoma were discussed. 3H-TdR autoradiography showed that carcinoma cells have a longer generation time, thus effecting mitosis, than normal proliferating cells; this generation time was thought to be about 3-7 days for cancer cells compared to 24-30 hr for normal cells. Due to prolongation of cancer cell life, there are no extreme variations in the growth fraction, and cancer cells have incidental destruction. That is to say, this type of cell death is not due to maturation but rather to sudden death of the mitotic cell due to malignant change in the surrounding stroma. The time it takes for a cancer to double its vol is about 1-3 mo for human cancers in general and about 1 yr to several yr for cancers of the large intestine. (26 Refs) (In JPN)

12. CARCINOEMBRYONIC ANTIGEN LEVELS IN THE DIAGNOSIS OF MALIGNANT LESIONS OF THE ABDOMINOPELVIC REGION.

Parente JT, Greston WM
Dept. Obstetrics and Gynecology, Bronx-Lebanon Hosp. Center, New York, NY
Surg Gynecol Obstet; 153(5):693-696 1981

The differential diagnosis of tumors of the abdominopelvic region can be difficult. The inability to differentiate carcinoma of the colon and rectum from carcinoma of the ovary, in particular, may result in inadequate surgical procedures and unnecessary complications. In this study, elevated pretreatment levels of carcinoembryonic antigen were used as an aid in distinguishing between extragenital and gynecologic tumors in 76 women. Levels below 10 nanograms per ml suggested a malignant tumor of the female reproductive tract or benign disease; levels above 20 nanograms per ml indicated carcinoma of an extragenital organ. In addition to other diagnostic studies, pretreatment values of carcinoembryonic antigen may enable the physician to anticipate the specificity of the tumor and the scope of the surgical problem more precisely and, thus, be better able to prepare the patient for optimum treatment. (Author abstract) (8 Refs)

13. CEA AS A CANCER MARKER.

Goldenberg DM, Neville AM, Carter AC, Go VL, Holyoke ED, Isselbacher KJ, Schein PS, Schwartz M
Univ. Kentucky Medical Center, Lexington, KY
Conn Med; 45(11):735-737 1981

Conclusions and recommendations regarding the tumor marker carcinoembryonic antigen (CEA) made during a Consensus Development Conference are presented. The upper limit of normal for CEA levels in plasma is 2.5 nanog/ml. Higher values may be associated with cancers (particularly of the gastrointestinal tract, pancreas, ovary, lung, and breast) but are also found in cigarette smokers, patients with benign tumors, and with inflammatory disorders, liver disease, and lung infections. CEA does not possess the sensitivity or specificity required to discriminate between localized malignant tumors and benign disorders. Grossly elevated values (5-10x normal), however, are strongly suggestive of cancer. Since preoperative CEA levels in patients with colorectal or possibly bronchial carcinomas can be indicative of survival rate, CEA values may be used in these cases in addition to clinical and pathological staging methods. Regular assay of CEA in postoperative colorectal cancer patients is the best method for detecting recurrence. The role of CEA in postoperative and therapeutic monitoring of other types of cancers is less convincing. Clinical utility of a tumor marker may be related to the efficacy of a therapeutic regimen. As more successful treatments for major tumor types become available, CEA and other tumor markers may become more useful in the management of cancer. (no Refs)

14. THE IMPORTANCE OF LECTIN BINDING SITES AND CARCINOEMBRYONIC ANTIGEN WITH REGARD TO NORMAL, HYPERPLASTIC, ADENOMATOUS, AND CARCINOMATOUS COLONIC MUCOSA.

Klein PJ, Osmers R, Vierbuchen M, Ortmann M, Kania J, Uhlenbruck G
Pathologisches Institut, Universitat Koln, Josef-Stelzmann-Strasse 9, D-5000 Koln 41, W. Germany
Recent Results Cancer Res; 79:1-9 1981

Lectin and carcinoembryonic antigen (CEA) binding sites were studied in normal and tumorous colonic mucosae. Tissue samples included 15 macroscopically normal margins from colonic carcinoma patients, 26 transitional mucosa samples, 3 hyperplastic polyps, 16 adenomas, and 33 colonic carcinomas of various degrees of differentiation. Normal and carcinomatous mucosae differed mainly in number of binding sites for various lectins and anti-CEA antibodies; staining was therefore not tumor-specific. Transitional mucosa had higher levels of lectin and CEA binding sites and higher production of mucinous substances than normal mucosa. Adenomatous mucosa exhibited similar characteristics, but lectin binding sites were reduced in proliferating areas. Lectin binding sites varied in number among carcinoma samples, increasing in partial relationship with the degree of tumor differentiation. CEA and Ricinus communis agglutinin binding sites frequently showed similar distributions in carcinoma samples. Peanut agglutinin binding sites were present only in transitional and carcinomatous mucosae. Results suggest that a disturbance in production or in composition of mucosal glycoproteins of the colon may reflect an initial phase of colonic cancer; lectins in the diet may affect cell proliferation, an essential factor of tumorigenesis. (25 Refs)

15. STUDIES ON CELL-MEDIATED IMMUNITY IN PATIENTS WITH COLORECTAL CANCER: LEUCOCYTE MIGRATION INHIBITION TEST USING ALLOGENIC 3M KCL EXTRACT.

Kojima O, Fujita Y, Iwai N, Yamane T, Kitagawa N, Nishioka B, Majima S
1st Dept. Surgery, Kyoto Prefectural Univ. Medicine, Hirokoji, Kawaramachi, Kamigyo, Kyoto 602, Japan
Aust NZ J Surg; 51(5):434-439 1981

Leukocytes from patients with colorectal and other malignant and non-malignant gastrointestinal diseases as well as those from normal subjects were tested by the leukocyte migration inhibition test (LMIT), employing the method of Clausen, using five different allogenic 3M KCl soluble extracts of colorectal cancer tissue. The normal range of migration index (MI) was found to be greater than 0.82 and less than 1.20 by calculating the mean MI +-2SD of 10 normal subjects with cancer extracts. Mis out of this range were considered to be pathological. In LMIT with a single tumor extract, a pathological MI was found in 46% of 50 colorectal cancer patients, a significantly higher figure than found in the three other groups of patients (4% to 16%). In the panel mode of LMIT, that is, testing each blood sample with five different tumor extracts, 40/50 (80%) of patients with colorectal cancer were reactive, while 2/15 (13%) of gastric cancer patients showed a 'positive' reaction; no positive reactivity was observed in the other two groups of patients. Thus 'positive' reactivity was significantly commoner in patients with colorectal cancer than in patients belonging to the other groups. The frequency of 'positive' reactivity was higher in patients with Dukes C carcinoma than in those with Dukes A or B carcinomas, though differences were not significant. In the follow-up study, marked depression of reactivity was seen 10 to 14 days after curative resection. In patients without recurrence, leukocyte migration was found to be in the normal range during the 2 to 4 wk after surgery. 'Positive' reactivity reappeared in patients with local recurrence. Thus the LMIT, particularly when tested by a panel mode, by demonstrating cell-mediated immunity against tumor-associated antigens of colorectal cancer, provides a method of monitoring colorectal cancer activity. (Author abstract) (13 Refs)

16. IMMUNITY OF PATIENTS WITH LARGE INTESTINE CANCER.

Watanabe T, Higuchi Y, Moritani Y, Iwado T, Matsui T, Hamazaki K, Fuchimoto S, Miwa H, Mannami T, Konaga E, Mimura H, Orita K
First Dept. Surgery, Okayama Univ. Sch. Medicine, Okayama, Japan
Nippon Rinsho; 39(5):42-46 1981

Parameters to study and assess the status of immunity in patients with cancer of the large intestine were discussed. The most basic tests of immunity for patients with large intestine cancer were thought to be cytotoxic T cell (Tc) activity against tumor specific antigen (TSA) and the delayed hypersensitivity initiation T cell response to TSA. Pre- and postoperative Tc tests performed in 107 patients with large intestine cancer showed significant postoperative drops in cytotoxicity indices corresponding to tumor Stages I-IV, but patients with Stage V tumors showed significantly increased cytotoxicity. This increase suggested recurrence or metastasis. Positive macrophage inhibition tests have been observed in large intestine cancer patients to the degree of those observed in patients with gastric cancer. Positive leukocyte inhibition tests have been shown to correlate with high 3-yr survival rates in patients with large intestine cancer; rates of positive leukocyte adherence inhibition tests are correlated with Dukes' classification of large intestinal cancer. Delayed skin response tests correlate with the stage of large intestine cancer and can be used to assess postoperative immune status. Positive purified protein derivative tests correlated to less advanced stages of large intestine cancer. Lymphoblastic transformation tests, peripheral lymphocyte counts, antibody-dependent cell-mediated cytotoxicity tests, natural killer cell activity, blocking factor, and immunosuppressive acid protein have been used to assess the stage of the tumor and/or immune status of patients with cancer of the large intestine. In large intestine cancer patients, the higher the stage of the tumor the lower the non-specific cellular immunity and the greater the amount of immune blocking factors. On the other hand, the higher the stage of the tumor, the lower the specific immunity to TSA. To the degree that immunity is preserved, the prognosis is good. (30 Refs) (In JPN)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

17. LUMBOPELVIC LYMPHADENECTOMY IN TREATMENT OF RECTAL CANCER.

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Dept. Gastrointestinal Tumors, N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Vestn Khir; 127(9):63-65 1981

Lumbopelvic lymphadenectomy was carried out in 64 patients (34 men, 30 women; 52 were greater than 40 yr old) with rectal cancer. Three of these patients underwent Hartmann operation, 3 underwent transabdominal resection of the rectum, 21 underwent abdominal-anal resection, and 37 underwent abdominal-perineal extirpation. Prior to extended surgery, all patients were subjected to direct inferior lymphography. The lymphographic examination indicated the presence of metastases in 23 of the patients. Histological examination of removed lymph nodes showed metastases in 12 of the patients. Of the 23 patients with positive lymphographic findings, only 10 had histologically confirmed metastases. Histological examination confirmed the absence of metastases in 39/41 patients for whom the lymphographic findings were negative. (6 Refs) (In RUS)

18. LYMPH NODE METASTASES FROM CARCINOMAS DEVELOPING IN PEDUNCULATED AND SEMIPEDUNCULATED COLORECTAL ADENOMAS.

Kodaira S, Teramoto T, Ono S, Takizawa K, Katsumata T, Abe O
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Aust NZ J Surg; 51(5):429-433 1981

Intramucosal carcinomas do not metastasize, but 5% to 10% of patients with submucosal cancers show lymph node involvement. Some of these submucosal cancers occur in pedunculated or semipedunculated polyps, which are usually treated by endoscopic polypectomy. Of 214 colorectal polyps removed endoscopically at the Keio University Hospital from 1976 to 1979, 6 showed submucosal invasive carcinoma. All six patients were subjected to colon resection, and two were found to have lymph node metastases. Consideration of these cases and of the literature suggests that resection is necessary after endoscopic polypectomy when there is carcinoma at the cut end, massive carcinomatous invasion of the neck of the polyp, lymphatic involvement, or poorly differentiated adenocarcinoma. (Author abstract) (9 Refs)

19. SINGLE-LAYER CONTINUOUS COLORECTAL ANASTOMOSIS.

Bailey HR, La Voo JW, Max E, Smith KW, Hampton JM
250 Hermann Professional Building, Houston, TX, 77030
Aust NZ J Surg; 51(5):473-476 1981

Since the first successful resection of a colonic neoplasm was carried out in 1823, many attempts have been made to find the ideal technique for bowel anastomosis, in respect both of the surgical technique employed and the suture material used. We have finally adopted a single layer anastomosis with a continuous polypropylene suture. To our knowledge, no series of such anastomoses has so far been reported, and we now review our technique, first described by Allen in 1979, and our very satisfactory experiences following our adoption of it for virtually all colorectal anastomoses above the peritoneal reflection. (Author abstract) (19 Refs)

20. TRENDS IN THE UNITED STATES FOR THE MANAGEMENT OF ADENOCARCINOMA OF THE RECTUM.

Mettlin C, Mittleman A, Natarajan N, Murphy GP, Schmitz RL, Smart CR
Dept. Cancer Control and Epidemiology, Roswell Park Memorial Inst., Buffalo, NY
Surg Gynecol Obstet; 153(5):701-706 1981

Data from surveys conducted by the Commission on Cancer of the American College of Surgeons were examined to identify recent trends in the treatment of carcinoma of the rectum.

Between 1973 and 1978, the stage of disease at diagnosis for the total series changed little, but significant upgrading in the stage of disease at diagnosis for the black patients was observed. There was increasing use of a multimodality approach to treatment combining operation with radiotherapy. The use of chemotherapy alone or in combination with other therapies, while never widely used, declined during the interval observed. Significant changes occurred in the type of operations performed for carcinoma in the upper two-thirds of the rectum. During this interval, abdominoperineal resection was increasingly being displaced by low anterior resection. The trend toward multimodality treatment and the use of effective sphincter preserving procedures represent significant changes noted in this survey in the therapy of carcinoma of the rectum. (Author abstract) (10 Refs)

21. EFFECT OF CLINDAMYCIN PROPHYLAXIS ON THE COLONIC MICROFLORA IN PATIENTS UNDERGOING COLORECTAL SURGERY.

Kager L, Liljeqvist L, Malmborg AS, Nord CE
Dept. Surgery, Huddinge Univ. Hosp., Karolinska Inst., Stockholm, Sweden
Antimicrob Agents Chemother; 20(6):736-740 1981

Clindamycin was given iv to 15 patients undergoing colorectal surgery in an initial dose of 600 mg, given at induction of anesthesia followed by six doses of 600 mg at 8-hr intervals. Series of serum samples and fecal specimens were taken for analysis of clindamycin concentrations. Tissue samples from the gut wall were taken at surgery. The highest serum concentrations observed occurred 30 min after administration of clindamycin and varied between 6.8 and 37.9 ug/ml (mean, 14.8 +-2.0 [standard error] ug/ml). The clindamycin concentrations in the tissue samples were between 1.8 and 13.0 ug/g. Clindamycin concentration in the fecal samples varied between 2.1 and 460 ug/g. Fecal samples were also collected during the investigation period for cultivation of aerobic and anaerobic bacteria. Among the aerobic bacteria, enterococci and streptococci decreased during the prophylaxis period. Anaerobic bacteria also decreased significantly during the same period. After the clindamycin administration period, enterococci, streptococci and anaerobic bacteria proliferated. No anaerobic strains resistant to clindamycin were isolated. Postoperative infections due to Streptococcus faecalis and different enterobacteria such as Escherichia coli, Enterobacter cloacae, Citrobacter freundii, and Klebsiella pneumoniae occurred in five patients. (Author abstract) (18 Refs)

22. A CONTROLLED PROSPECTIVE TRIAL OF ADJUVANT RAZOXANE IN RESECTABLE COLORECTAL CANCER.

Gilbert JM, Cassell PC, Ellis H, Wastell C, Hellmann K, Evans MG, Stoodley BJ
Clinical Res. Center, Watford Road, Harrow, Middlesex HA1 3UJ, England
Recent Results Cancer Res; 79:48-58 1981

Razoxane was tested as an adjuvant chemotherapeutic agent for treatment of colorectal cancer. A total of 162 patients were classified by Duke's system as Group A (31), Group B (49), Group C (61), or Group D (17). An additional four patients were randomized in error. Chemotherapy consisted of 125 mg razoxane po bid, 5 days/wk indefinitely. Treatment was reduced or stopped when WBC count fell to less than 3,000/cubic mm. After 3 yr 134 patients were evaluated. When all four groups were analyzed together, differences between razoxane-treated patients and controls were distorted. Groups A and D were excluded, as surgery alone may have been curative in Group A, and Group D included advanced, unresponsive tumors. Median time to recurrence for Group B was 5 mo for controls and 16 mo for treated patients. For Group C the interval was 6 mo for controls and 12 mo for treated patients. Recurrences, usually within 1 yr of the start of treatment, were more frequent among controls. No significant toxicity was produced by razoxane, particularly at the lower doses required for continuous treatment. (15 Refs)

23. FUNDAMENTAL AND CLINICAL STUDIES ON ORAL AND RECTAL ADMINISTRATION OF ANTICANCER AGENTS: MAINLY IN REGARD TO N1-(2'-TETRAHYDROFURYL)-5-FLUOROURACIL (FT-207).

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First Dept. Surgery, Sch. Medicine, Fukuoka Univ., Nishi-ku, Fukuoka 814, Japan
Fukuoka Daigaku Igaku Kiyo; 8(2):187-199 1981

Since there are few reports on the concentration of anticancer drugs in the tumor, FT-207 was used to study drug concentrations in the blood, organs and tumors in experimental animals and in patients. FT-207 was administered continuously po to two groups of Donryu rats, with and without AH-1 30 cancer. The uptake by various organs and the distribution in tumor tissue of FT-207 and its active substance 5-fluorouracil (5-FU) were good in both groups. There was no significant difference in 5-FU concentration in organs of healthy rats and organs and tumors of cancer-bearing rats. There was not significant difference in FT-207 concentration in the blood and tissue of J-W rabbits after oral or rectal administration. However, rectal administration caused a significantly higher concentration of 5-FU in the portal blood, esophagus, stomach, muscle, urinary bladder, bile, abdominal lymph nodes, cervical lymph nodes, testis and fat (p less than 0.05). Eighty-seven patients, mainly with gastric cancer, were divided into two groups, one given FT-207-enteric-coated granules po and the other given FT-207 suppositories. Blood and tissue concentrations were determined after 3 days of administration of two single doses of 750 mg of FT-207 per day. The concentrations of FT-207 and 5-FU did not differ significantly between the two groups. The uptake of 5-FU was good in the tumors of any organ. The level was low in breast, gastric, colon and rectal cancer, in decreasing order, after po administration, and in gastric, breast, colon and rectal cancer, in decreasing order, after rectal administration. These results are generally consistent with other reports on clinical effects. A study of 5-FU levels in tumors according to the degree of tumor differentiation in 51 cases of gastric adenocarcinoma revealed no significant differences. (33 Refs) (In JPN)

24. LIGATION AND CATHETERIZATION OF HEPATIC ARTERY IN CHEMOTHERAPY OF PRIMITIVE AND SECONDARY HEPATIC TUMORS.

Lesti G, Andriani G, Marinucci R
Istituto di Patologia Speciale Chirurgica, Universita di Chieti, Chieti, Italy
Ann Ital Chir; 53(2):191-204 1981

Hepatic artery ligation (HAL) was studied in primary (P) and secondary not resectable hepatic (H) tumors (T) in association with their resection, and in H metastases. Contraindication for HAL was portal insufficiency due to advanced liver cirrhosis, jaundice, T invasion of greater than than 30% of H parenchyma, pronounced cachexia, widespread metastatic diffusion, and renal insufficiency. Tests performed before and after surgery, as well as surgical technique were presented. The eight patients (40-65 yr old, 1 female and 7 male) studied had: hepatoma of right lobe, gallbladder T invading liver, and six liver metastases (P colon cancer in 5 cases and in 1 case P ovarian cystoma). Seven days after HAL, cytostatic therapy with 5-fluorouracil was initiated and repeated every wk in hospital, at home or in ambulatory care, starting with 1 g and decreasing to 500 mg due to deteriorating hematologic status. Patients with liver metastases from P colon cancer survived 7-12 mo. The patient with gallbladder cancer invading the liver, died 6 mo later. The hepatoma patient survived 3 mo. Still living and surviving more than 2 yr after HAL, was the patient with liver metastases after P ovarian cystoma. Five mo after HAL, in two cases the catheter spontaneously came out. Necrosis of liver parenchyma was evident one day after HAL. There was regression of T and liver mass. Direct infusion by portal way was anticipated. (28 Refs) (In ITA)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

25. OBTAINING HOSPITAL AND PHYSICIAN PARTICIPATION IN A CASE-CONTROL STUDY OF COLON CANCER.

Herrmann N, Amsel J, Lynch E
Dept. Res. Medicine, Univ. Pennsylvania, Nursing Education Building, 420 Service Dr. S2, Philadelphia, PA, 19104
Am J Public Health; 71(12):1314-1319 1981

This paper describes efforts to solicit hospital and physician participation for a case-control study of the etiology of colon cancer in five Pennsylvania counties of the Philadelphia metropolitan area. Forty-seven of the 70 hospitals in this region were eligible for inclusion in the study. Thirty-seven (79%) agreed to participate, 27 of them within 6 mo of initial contact. The median time to approval of participation was 3 mo and the median number of separate contacts was nine. At least five participating hospitals submitted the protocol to their lawyers and nine required that special procedures be developed for release of patient information. Two hundred fourteen of 256 listed attending physicians were eligible for participation; 161 (75%) permitted all patients to be contacted; 23 (11%) permitted some patients to be contacted; 30 (14%) refused all patient contact. A significant association between type of specialty and type of permission was found (p approx = 0.005). Concerns about confidentiality and lack of personal advantage were frequently cited by non-participants. The validity of case-control studies relying on hospital or physician ascertainment of cases is seriously challenged by such lengthy delays and lack of participation which can result in a biased pool of potential cases. (Author abstract) (10 Refs)

26. EPIDERMOID CARCINOMA COMPARED WITH ADENOCARCINOMA OF THE ANAL CANAL.

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Aust NZ J Surg; 51(5):426-429 1981

Sixty-five cases of anal carcinoma have been treated in the past 20 yr -44 adenocarcinomas, 15 epidermoid carcinomas and 6 others. The sex ratio of male to female was 2:13 among those with epidermoid carcinoma and 27:17 in the adenocarcinoma group. There was no significant difference between the 5-yr survival associated with both kinds of carcinoma, though adenocarcinomas invaded more deeply and were larger. Lymph node metastases were found in 60% of cases in each group, but inguinal metastases were found in 47% of epidermoid carcinomas and 32% of adenocarcinomas; lung and liver metastases were seen in 13 % of the former and 18% of the latter (there was no statistical significance). A new staging is proposed, supported by the 5-yr survival rate (in parentheses), as follows: Stage I - T1, T2, N0, M0 (100%); Stage II - T3, T4, N0, M0 (66.7%); Stage III - any T, N1, M0 (31.6%); Stage IV - any T, any N, M1 (0%). (Author abstract) (5 Refs)

27. CARCINOMA OF THE COLON AND RECTUM WITH LIVER INVOLVEMENT.

Boey J, Choi TK, Wong J, Ong GB
Dept. Surgery, Univ. Hong Kong, Queen Mary Hosp., Hong Kong, Hong Kong
Surg Gynecol Obstet; 153(6):864-868 1981

The records of 126 patients with adenocarcinoma of the colon and rectum who presented with liver involvement were reviewed. Prognosis was determined by the amount of metastases to the liver, which was usually extensive if ascites or a raised alkaline phosphatase level was present. The longest survival period was achieved with resection of the primary tumor along with hepatic lesions confined to a single lobe, especially those due to direct tumor infiltration. If liver deposits were found bilaterally, palliative resection of the primary lesion relieved intestinal symptoms. This may also prolong the survival time, because a fixed primary tumor appeared to diminish the outlook among patients with comparable liver disease. Palliative resection in the presence of ascites resulted in a high mortality, and the survival rate was no better than that after diversion procedures. We recommend resection without anastomosis for carcinoma of the rectosigmoid in patients with ascites and unresectable secondary lesions of the liver. (Author abstract) (5 Refs)

28. CAUSES OF HEPATIC METASTASIS AND RECURRENCE OF CANCER IN THE LIVER AND PREVENTING THEM.

Takahashi T, Furushima K, Takahashi T, Tamura S, Ohta H
Dept. Surgery, Cancer Res. Inst. Affiliated Hosp., 1-37-1 Kami-ikebukuro, Toshima-ku, Tokyo 170, Japan
Nippon Rinsho; 39(5):154-161 1981

Incidence and treatment of hepatic metastasis and recurrence was studied in 381 patients with colon cancer and 714 patients with rectal cancer who were treated surgically. Hepatic metastasis was observed in 49 patients with colon cancer and 72 patients with rectal cancer. Of the 49 patients with hepatic metastasis and colon cancer, 23 had primary tumors greater than 5 cm, 30 had circumferential tumors, 41 had lymph node metastasis, and 29 had clear evidence of intestinal wall invasion. Of the 72 patients with hepatic metastasis and rectal cancer, 38 had primary tumors greater than 5 cm, 37 had circumferential tumors, 58 had lymph node metastasis, and 39 had clear evidence of intestinal wall invasion. Histological examination of tumor specimens from 290 patients with colon cancer and 578 with rectal cancer showed that papillotubular cancer was the type most frequently observed in patients with hepatic metastasis. Cause s of the hepatic metastasis were thought to be (1) distribution of cancer cells during surgery via the portal vein, (2) micro-tumors already existing in the liver prior to surgery, or (3) residual tumor or recurrent tumor causing secondary formation of hepatic metastasis. Prevention of blood-born metastasis with combination chemotherapy has not been successful thus far. (5 Refs) (In JPN)

29. OOPHORECTOMY IN WOMEN WITH CARCINOMA OF THE COLON AND RECTUM.

O'Brien PH, Newton BB, Metcalf JS, Rittenbury MS
Dept. Surgery, Medical Univ. South Carolina, Charleston, SC
Surg Gynecol Obstet; 153(6):827-830 1981

Carcinoma of the colon and rectum metastasizes readily to the ovaries, and oophorectomy during operation upon the colon and rectum remains an effective surgical technique for precluding subsequent oophorectomy and, thereby, diminishing the morbidity of carcinoma of the colon and rectum in women. This procedure does not significantly affect the survival rate. Carcinoma of the ovary has become the fourth most common lethal cancer in women. Usually, the tumor is diagnosed after the development of ascites, mass and wt loss. The 5 yr survival rate remains about 30%. The incidence of carcinoma of the ovary in women with carcinoma of the colon and rectum is roughly 5x the incidence of carcinoma of the ovary, that would be expected by chance. We believe the aforementioned observations strongly expand and reinforce the original proponents of prophylactic oophorectomy performed upon women with carcinoma of the colon and rectum and that, therefore, oophorectomy should be an integral part of operation upon the colon and rectum in women. (Author abstract) (17 Refs)

30. OVARIAN INVOLVEMENT IN ADENOCARCINOMA OF THE COLON AND RECTUM.

Blamey S, McDermott F, Pihl EI, Price AB, Milne BJ, Hughes E
Dept. Surgery, Monash Univ., Alfred Hosp., Prahran, Victoria, Australia
Surg Gynecol Obstet; 153(1):42-44 1981

Thirty-six of 998 female patients with carcinoma of the colon and rectum had ovarian involvement at the time of the initial operation. Resection of tumors of the colon and rectum were performed upon 882 patients. The ovarian tumors were removed in 30 of the 36 patients with ovarian involvement. Ovarian involvement was associated with a significantly worsened ($p = 0.009$) cancer specific 5 year survival rate; 5 year survival prospects for patients with, and without, ovarian involvement were 38 and 60%, respectively. Ovarian involvement also significantly ($p = 0.014$) worsened the survival rate of the 25 patients treated by curative resection of the tumor of the colon and rectum and associated ovarian spread. The 5 yr cancer specific survival rate for female patients without ovarian involvement was 72%, whereas ovarian involvement reduced the survival rate to 50%. (Author abstract) (13 Refs)

31. ELEMENT DIETS IN PREOPERATIVE MANAGEMENT OF PATIENTS UNDERGOING SURGERY OF THE LARGE INTESTINE.

Skobelkin OK, Morev AI
Moscow, USSR
Khirurgiia (Mosk); (9):83-85 1981

Element diet was used in the preoperative management of 54 patients undergoing surgery of the large intestine. Use of a formulation (Complan) containing the essential nutrients improved the functional state of the liver and reduced the number of postoperative complications (6.2%, compared with 13.2% in patients who did not receive the element diet). (11 Refs) (In RUS)

32. RECENT RESULTS OF CLINICAL THERAPEUTIC TRIALS FOR GASTROINTESTINAL MALIGNANCIES CONDUCTED IN THE UNITED STATES.

Kisner DL, Schein PS, Macdonald JS
Div. Cancer Treatment, Cancer Therapy Evaluation Program, NCI, Bethesda, MD
Recent Results Cancer Res; 79:28-40 1981

Current clinical therapeutic trials of treatment for gastrointestinal cancer are reviewed. The trials have been aimed at identifying active single chemotherapeutic agents (CA), combining modalities in treatment of locoregional disease, and introducing active therapies into surgical adjuvant use. Drugs active against advanced gastric cancer include 5-fluorouracil (5-FU), mitomycin C (MM-C), 1,3-bis(2-chloroethyl)-1-nitrosourea, adriamycin (ADM), and cis-platinum. Combinations of CA appear more effective than single agent therapy. Against locally advanced gastric tumors, CA alone produce longer survival times than CA plus radiation therapy, but combined therapy has a long-term benefit. Agents active against pancreatic carcinoma include 5-FU, MM-C, streptozotocin, and ADM. Radiation therapy with 5-FU appears more effective than radiation alone. Toxic effects have been produced by 5-FU. Research into treatment of colorectal carcinoma (CRC) should be directed at identifying new active agents, since those already studied have produced limited benefits. The value of chemotherapy as an adjuvant to surgery in CRC is uncertain. Some favorable results have been obtained with nonsurgical therapies. (41 Refs)

33. MULTIPLE METACHRONOUS GASTRO-INTESTINAL CARCINOMA.

Brownstein EG
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Aust NZ J Surg; 51(5):445-450 1981

A patient who developed multiple metachronous gastro-intestinal carcinoma is described. This patient has had multiple invasive carcinoma of the colon, jejunum and stomach over a 34-yr period, commencing at the age of 44 yr. All the colonic tumors have been Duke's A Grade, although penetration has occurred to the serosal level. The family pedigree of the propositus shows an autosomal Mendelian dominant gene pattern with a characteristic early age of onset and a significant frequency of multiple metachronous primary malignant neoplasms. Identification of this syndrome provides an opportunity to include in a surveillance program, those unaffected patients in the pedigree who have an extra risk of early development of cancer at specific sites. (Author abstract) (10 Refs)

34. PRIMARY ADENOCARCINOMA OF AN ANAL GLAND WITH SECONDARY PERIANAL FISTULAS.

Lee SH, Zucker M, Sato T
Lab. Service, Veterans Admin. Medical Center, 4801 Linwood Blvd., Kansas City, MO, 64128
Hum Pathol; 12(11):1034-1036 1981

A case of primary mucinous (colloid) adenocarcinoma associated with multiple perianal fistulas and a supra-anal inter-gluteal abscess of a short duration is described. The origin of this tumor has been much debated. Some believe that the tumor occurs primarily in an anal duct or its glands with secondary fistula formation whereas others claim that the tumor arises in a chronic fistulous tract. The present study substantiates the former concept on the basis of the mode of clinical presentation and the pathologic findings of a large tumor, without involvement of the anorectal mucosa. The residual anal ducts and glands were found in close relationship with the tumor. (Author abstract) (28 Refs)

35. ACTIVITY OF 9-10 ANTHRACENEDICARBOXADLEHYDE BIS[(4,5-DIHYDRO-1 H-IMIDAZOL-2-YL)HYDRAZONE]DIHYDROCHLORIDE (CL216,942) IN A HUMAN TUMOR CLONING SYSTEM. LEADS FOR PHASE II TRIALS IN MAN.

Von Hoff DD, Coltman CA, Forseth B
Dept. Medicine, Div. Oncology, Univ. Texas Health Science Center at San Antonio, San Antonio, TX, 78284
Cancer Chemother Pharmacol; 6(2):141-144 1981

The anthracene derivative 9-10 anthracenedicarboxaldehyde bis[(4,5-dihydro-1 H-imidazol-2-yl) hydrazone]dihydrochloride (CL216,942) was screened for antitumor activity against a human tumor cloning system; 273/684 cultured specimens of human tumors were evaluable for drug sensitivity information. Distinct heterogeneity of tumor sensitivity to CL216,942 was observed. For some tumors, a more profound decrease in tumor colony forming units (T-CFU) was observed with increasing drug concentrations. For others a plateau in the survival curve even with increasing concentrations of CL216,942 was noted. CL216,942 demonstrated greater than or equal to 70% decrease in T-CFU with at least two different patient tumors for breast cancer, small cell and squamous cell lung cancer, lymphoma, melanoma, ovarian cancer, pancreatic cancer, and renal cell cancer. The drug gave a greater than or equal to decrease in T-CFU against at least one tumor for adenocarcinoma of unknown origin, adrenal cancer, head and neck cancer, large cell lung cancer, leukemia, and gastric cancer. If a greater than or equal to 70% decrease in tumor kill is used to define activity, CL216,942 was definitely inactive in vitro against colorectal carcinoma. Not enough evaluable tumor specimens of the other histologic tumor types were available to determine CL216,942 activi ty. The data indicate that CL216,942 has a wide spectrum of in vitro antitumor activity. (10 Refs)

36. IN VITRO EVALUATION OF ANTICANCER DRUGS WITH THE HUMAN TUMOR STEM CELL ASSAY.

Salmon SE, Von Hoff DD
Univ. Arizona Cancer Center, Tucson, AZ, 85724
Semin Oncol; 8(4):377-385 1981

The development and use of in vitro soft agar colony assays for human tumor stem cells (HTSC) in preclinical drug screening for active compounds, clinical trials of new agents, and final selection of treatment for individual patients are discussed. Methods of cell culture and measurement of drug sensitivity are described. The HTSC assay grows a variety of tumor types from many sources. The success of growing particular tumors is variable and depends on both tumor type and source of the tumor specimen. Five approaches used to show the neoplastic origin of agar colonies from tumor biopsies include light and electron microscopy, chromosome marker studies, tumor markers, and injection of cells from colonies into nude mice. The HTSC assay has been accurate in predicting what drug will not work against an individual patient's tumor and is promising for predicting what drug will work. Examples of standard and new drugs tested in vitro against different types of cancer with the HTSC assay are presented. Use of the HTSC assay for testing cis-platinum against neuroblastomas, dihydroxyanthracenedione against small cell lung cancer, and methylglyoxal bis guanethylhydrazone against colorectal cancer is reported. (24 Refs)

37. ALTERATION OF THE SURVIVAL RESPONSE OF TWO HUMAN COLON CARCINOMA SUBPOPULATIONS TO X-IRRADIATION BY N,N-DIMETHYLFORMAMIDE.

Leith JT, Gaskins LA, Dexter DL, Calabresis P, Glicksman AS
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Cancer Res; 42(1):30-34 1982

Two subpopulations of tumor cells obtained from a single human colon adenocarcinoma have been examined with regard to their intrinsic sensitivity to x-irradiation and to how this intrinsic radiosensitivity might be altered by growth in the polar solvent, N,N-dimethylformamide (DMF). These subpopulations, designated clones A and D, differ significantly in their radiation sensitivity. Using the single-hit multitarget equation to fit the survival responses, clone A exhibited survival parameters: extrapolation number (n) = 6.3; quasi-threshold dose (Dq) = 2.50 Grays; and mean lethal dose (Do) = 1.36 Grays. These parameters for clone D were: n= 2.3; Dq = 1.27 Grays, and Do = 1.56 Grays. Alteration of intrinsic radiosensitivity by DMF was then studied by adapting colon tumor cells to continuous growth in Roswell Park Memorial Institute Tissue Culture Medium 1640 containing 0.8% DMF. This treatment promotes differentiation of these colon cancer cells and is associated with an increased cell culture doubling time of 50 hr (20 hr for cont rol cultures). It was found that, for cells grown in DMF medium, irradiated in fresh complete medium, and replated into fresh complete medium, survival parameters were: clone A - n = 5.2, Dq = 1.91 Grays, and Do = 1.15 Grays; clone D - n = 2.2, Dq = 0.96 Grays, and Do = 1.21 Grays. For tumor cells grown in DMF medium, irradiated in fresh complete medium, and replated into medium containing 0.8% DMF, survival parameters were: clone A - n = 2.8, Dq = 1.07 Grays, and Do = 1.03 Grays; clone D - n = 2.0, Dq = 0.82 Grays, and Do -1.19 Grays. Survival responses of cells grown in fresh complete medium, irradiated in fresh complete medium, and replated into medium containing 0.8% DMF were not different from control responses. Using the Dq as an index of the sensitization occurring in the clinically relevant dose range, the pretreatment in DMF medium sensitizes both clone A and D cells to subsequent x-irradiation by a factor of approx 1.3, whereas pre- and posttreatment in DMF medium increases this factor for clone A to 2.3 and for clone D to 1.5. Therefore, growth of colon cancer cells in DMF medium prior to irradiation, which results in cell differentiation, actually increases the sensitivity of cells to x-rays. Furthermore, subsequent reculturing of irradiated cells in DMF-containing medium compared to regular growth medium results in a further augmentation of the response. (Author abstract) (20 Refs)

38. LETHAL ACTIVITY AND KINETIC RESPONSE OF CULTURED HUMAN CELLS TO 4'-(9-ACRIDINYLAMINO)METHANESULFON-M-ANISIDINE.

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Dept. Lab. Medicine, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Cancer Res; 42(1):107-111 1982

Cytotoxic and cytokinetic effects of 4'-(9-acridinylamino)methanesulfon-m-anisidine (m-AMSA) were studied on a cultured human colon carcinoma and on a human lymphoma (T1) cell line. Proliferating cells were more susceptible (10-fold) to the cytotoxic effect of m-AMSA than were nonproliferating cells. The agent had minimal effects on DNA synthesis. A comparable exposure doses on m-AMSA, the degree of lethal cell damage exceeded inhibition of DNA synthesis by four-fold. Cells synchronized in different stages of the cell cycle were equally sensitive to the cytotoxic effects of the drug, although the major cytokinetic effect was a block in G2. A greater killing effect was obtained by fractionated delivery than by a comparable dose delivered at once. These results suggest that superior antitumor results may be achieved by adequately spaced low doses of m-AMSA in the treatment of sensitive human tumors. (Author abstract) (34 Refs)

39. CYTOKINETIC AND BIOCHEMICAL EFFECTS OF 5-IMINODAUNORUBICIN IN HUMAN COLON CARCINOMA IN CULTURE.

Glazer RI, Hartman KD, Richardson CL
NCI, Building 37, Room 6D28, Bethesda, MD, 20205
Cancer Res; 42(1):117-121 1982

The semisynthetic anthracycline, 5-iminodaunorubicin (IM), was investigated to see whether modification of the benzoquinone moiety to produce a drug with low free radical potential would alter the cytotoxic and biochemical characteristics of this drug in comparison to Adriamycin (ADR), an agent with high free radical potential. Cell viability was measured in human colon carcinoma (HT-29) cells by soft-agar cloning. Upon exposure of either log-phase or early plateau-phase cells for 2 hr to IM or ADR, a threshold exponential cell lethality curve was obtained. Prolonging drug exposure to 24 hr produced an exponential decline in cell survival and a marked reduction in viability of both log-phase and early plateau-phase cells. Inhibition of DNA synthesis in log-phase cells after 2 and 24 hr of exposure to IM and ADR paralleled the increased cell lethality produced by the drugs. In contrast, total RNA synthesis was not inhibited by IM, whereas ADR impaired both RNA and DNA synthesis. Nuclear rRNA synthesis was not significantly inhibited following 24 hr of exposure to 10(-7) M ADR or IM but was inhibited by 85 and 35% at 10(-6) M ADR or IM, respectively. The affinity of IM and ADR for HT-29 DNA was measured in vitro by displacement of acridine orange binding and was found to be similar for both analogs. These studies suggest that the cytotoxicity of IM and ADR results from the interactions of these drugs with DNA. (Author abstract) (20 Refs)

40. CYTOKINETIC AND BIOCHEMICAL EFFECTS OF SANGIVAMYCIN IN HUMAN COLON CARCINOMA CELLS IN CULTURE.

Glazer RI, Hartman KD
NCI, Building 37, Rom 6D28, Bethesda, MD
Mol Pharmacol; 20(3):657-661 1981

The cytokinetic and biochemical effects of sangivamycin (SG) on human colon carcinoma in tissue were studied. Log phase and early plateau phase cells were exposed for 2, 24, and 48 hr to SG and cell viability was determined by soft agar cloning. Brief (2 hr) drug exposure of either log- or plateau-phase cells was not cytotoxic. Prolonging drug exposure to 24 or 48 hr dramatically increased cell lethality; 1 x 10(-6) M SG reduced cell viability of log phase cells by 83% and 97% after 24 and 48 hr of drug exposure, respectively, while cell viability was reduced in plateau-phase cells by 20% and 75%, respectively. Increasing the SG concentration to 1 x 10(-5) M increased cytoxicity only in plateau-phase cells. DNA synthesis was not significantly affected after 2 hr of drug exposure, but precipitously decreased following prolonged incubation with SG for 24 or 48 hr. In contrast, total RNA synthesis was initially inhibited up to 40% after 2 hr of exposure to 1 x 10(-5) SG, but was not reduced much further after longer intervals of drug treatment. RNA synthesis was not significantly inhibited in plateau-phase cells after 48 hr of drug exposure. In contrast, inhibition of non-poly(A)RNA and poly(A)RNA occurred to a degree comparable to that of total RNA in log-phase cells. The time and concentration dependence of SG incorporation into DNA and RNA correlated qualitatively with the effect of SG on cell viability. The incorporation of 3H-SG into poly(A)RNA correlated with the reduction in cell viability observed in log- and plateau-phase cells under comparable conditions. Results indicated that SG produces significant cell lethality to a human colon carcinoma which is generaly refractory to antitumor agents. (15 Refs)

41. HUMAN TUMOR XENOGRAFTS IN ATHYMIC NUDE MICE AS A PRECLINICAL SCREEN FOR ANTICANCER AGENTS.

Ovejera AA, Houchens DP

Battelle Columbus Lab., 505 King Ave., Columbus, OH, 43201

Semin Oncol; 8(4):386-393 1981

The role of the nude mouse-human tumor system in anticancer drug screening is discussed. Despite the possession of a small number of T cells, nude athymic mice are unable to reject skin grafts from widely divergent species. Successful xenotransplantation of human cancers to nude mice has provided an in vivo model for studying biologic characteristics of human tumors, especially response to therapy. Of the four most commonly studied tumor types, colorectal tumors and melanomas exhibit the highest rate of takes (greater than 60%), followed by lung tumors (approx 40-50%). Breast tumors are the most difficult to grow in nude mice: less than 20% of freshly implanted breast tumors are grown successfully. Breast (MX-1), colon (CX-1), and lung (LX-1) human tumor xenograft systems are included in the National Cancer Institute tumor panel. Chemotherapeutic responses of the three systems are described. The utility of human tumor xenografts for drug screening is discussed. (35 Refs)

42. HUMAN CANCERS TRANSPLANTED IN NUDE MICE RETAIN THE EXPRESSION OF THEIR ORGAN-SPECIFIC NEOANTIGENS.

Thomson DM, Neville AM, Phelan K, Schwartz Scanzano R, Vandevoorde JP

Montreal General Hosp., Montreal General Hosp. Res. Inst., 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada

Eur J Cancer Clin Oncol; 17(11):1191-1197 1981

Human cancers transplanted to nude mice seem to retain most features of the original tumor. To determine if organ-specific neoantigens were still expressed after transplantation, four different human cancers, supplied and coded by independent investigators, were assayed in the tube LAI assay. The LAI phenomenon measures the change in adherence properties of leukocytes that have bound an antigen to which they are sensitized immunologically. Four of four transplanted human cancers - pancreas, lung, breast, and colon - stimulated an LAI+ response with leukocytes from patients with cancers of the same organ. The antitumor response was not as vigorous against a pool of transplanted tumor extracts as against those prepared from liver metastases. Nonetheless, the results add to the mounting evidence that human cancers express neoantigens to which most humans bearing cancers respond immunologically. (Author abstract) (31 Refs)

43. EFFECT OF BETA-GLUCURONIDASE INHIBITOR ON AZOXYMETHANE-INDUCED COLONIC CARCINOGENESIS IN RATS.

Takada H, Hirooka T, Hiramatsu Y, Yamamoto M
Dept. Surgery, Kansai Medical Univ., 1 Fumizono, Moriguchi, Osaka, Japan
Cancer Res; 42(1):331-334 1982

In this study of the role of microfloral beta-glucuronidase in colonic carcinogenesis, the effect of beta-glucuronidase inhibitor was evaluated. Starting at 5 wk of age, male Donryu rats were fed either a semisynthetic diet or the same diet containing 0.1% beta-glucuronidase inhibitor as N-cyclohexyl-5-O-acetyl-2,4-O-(p-methoxybenzylidene)-D glucaro-1-amide-6,3-lactone (C-GAL). All animals were given sc injections of 7.4 mg azoxymethane (AOM) per kg body wt once a wk for 11 wk and followed for an additional 20 wk. Most animals receiving the colonic carcinogen developed tumors in the colon, and a few also developed tumors in the small intestine. However, the number of tumors in the large intestine of the rats given C-GAL at the same time as AOM was significantly lower than in the control rats, especially in the proximal half of the colon, but those given C-GAL after AOM treatment had almost the same number of colon tumors as did the controls. It is concluded that, since bacterial beta-glucuronidase activity in the feces of rats given 0.1% C-GAL was significantly inhibited, intestinal microfloral beta-glucuronidase may play an important role in colonic carcinogenesis caused by AOM. (Author abstract) (48 Refs)

44. THE EFFECT OF DISULFIRAM ON THE CARCINOGENICITY OF 3,2'-DIMETHYL-4-AMINOBIPHENYL IN SYRIAN GOLDEN HAMSTERS AND RATS.

Fiala ES, Weisburger JH, Katayama S, Chandrasekaran V, Williams GM
Naylor Dana Inst. for Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Carcinogenesis; 2(10):965-969 1981

Species differences in 3,2'-dimethyl-4-aminobiphenyl (DMAB) carcinogenicity, which induces mostly bladder tumors in Syrian hamsters and intestinal and breast tumors in rats, were investigated. Groups of male Syrian golden hamsters received sc injections of DMAB weekly for up to 22 mo (total av cumulative dose 555 mg) either alone or simultaneously with disulfiram in the diet. At the tolerated dose of disulfiram (2.5 mg/kg), the overall tumor yield induced by DMAB alone was not affected, but the number of small intestine tumors was reduced and the appearance of bladder and colon cancers was delayed. In two groups of male Charles River rats, weekly sc injection of DMAB (20 mg/kg) for 37 wk (total av cumulative dose 289 or 241 mg) induced primarily intestinal cancers. As in hamsters, addition of disulfiram to the diet of the second group reduced the incidence of small intestine cancers but resulted in the appearance of a small number of bladder cancers. DMAB-treated rats also developed in situ prostatic carcinoma, regardless of whether they were treated with or without disulfiram. (19 Refs)

45. THE IMMUNE RESPONSE TO CARCINOMA OF THE COLON IN A RAT MODEL: A TEMPORAL STUDY.

House AK
Queen Elizabeth II Medical Center, Nedlands 6009, Western Australia
Aust NZ J Surg; 51(5):487-493 1981

Carcinoma of the colon was induced in rats by treatment with 1,2-dimethylhydrazine (DMH). Macroscopic tumors were observed from 8 wk after commencing DMH injections and rapidly increased in mass to cause death of the animals between 20 and 27 wk later. Tumor immunity was assessed by the gross parameters of body, spleen and mesenteric lymph node weight and by in vitro tests of lymphocyte antitumor cytotoxicity and leukocyte migration inhibition by tumor and normal colon homogenates. Immune responses were recorded in control (saline treated) and in tumor (DMH treated) rats. Body wt of the tumor rats paralleled that of control animals until tumors were well advanced. At this time tumor animal body wt was significantly less than that of control animals. Spleen wt and in vitro lymphocyte antitumor cytotoxicity were significantly greater in tumor than in control rats and were so found soon after macroscopic tumors were observed. Mesenteric lymph node wt and leukocyte migration inhibition did not change until late in tumor development, but at this time there was an immune response in tumor animals. The study showed that carcinoma of the colon induced in rats was associated with an antitumor immune response and that this change occurred soon after macroscopic tumors were present. In spite of this the animals died of their neoplasms. (Author abstract) (27 Refs)

46. A STUDY ON CARCINOGENESIS INDUCED BY DEGRADED CARRAGEENAN ARISING FROM SQUAMOUS METAPLASIA OF THE RAT COLORECTUM.

Oohashi Y, Ishioka T, Wakabayashi K, Kuwabara N
First Dept. Pathology, Juntendo Univ. Sch. Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo, Japan
Cancer Lett; 14(3):267-272 1981

Carcinogenesis in the colorectum of F344 rats fed diets containing 10% degraded carageenan for varying lengths of time was investigated. After termination of carageenan administration, all rats were fed a basal diet until sacrifice 18 mo after initial administration. In males treated for 2 mo, the incidence of colorectal squamous metaplasia was 100%, with tumors in 5/39 animals. The tumors were squamous cell carcinoma, anaplastic carcinoma, and adenoma. In males treated for 6 mo, metaplasia was evident in 100% and 8/42 rats had tumors. In males treated for 9 mo, 100% of animals showed squamous metaplasia and 17/42 had tumors. No inflammatory or neoplastic changes were found in control animals. (10 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

47. EXTRACOLONIC CHANGES IN HEREDITARY ADENOMATOSIS OF THE LARGE INTESTINE.

Jirasek V, Chmel J, Balas V
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Cas Lek Cesk; 120(41):1239-1242 1981

Extracolonic changes were studied in 38 patients (from 17 families) with hereditary colonic adenomatosis. Skeletal changes were studied in 37 patients: endocraniosis was found in 22 cases, osteoma of the paranasal sinuses in 13, focal sclerosis and osteoma of the mandible in 14, cysts of the paranasal sinuses in 5, impacted teeth in 4, and changes in the long bones in 34. There were no skeletal changes in two cases. The gastroduodenoscopic findings, obtained in 26 cases, included solitary duodenal polyps (mostly adenomas) in six cases, multiple duodenal polyps in two, diffuse duodenal adenomatosis in one, diffuse gastric polyposis in six, and solitary hyperplastic polyp of the antrum in one. Extracolonic changes, most of them alike to Gardner's syndrome, were found in 92% of all patients. More than one type of extracolonic changes were present in 55% of the patients. The findings suggest that simple hereditary adenomatosis and Gardner's syndrome are one nosological entity, and that the differences found in the incidence of extracolonic changes are due to different expressivity of the dominant gene with a pleiotropic effect. (19 Refs) (In CZE)

48. LARGE INTESTINE CANCER AND HEREDITY.

Utsunomiya J
Second Dept. Surgery, Tokyo Medical and Dental Coll., Tokyo, Japan
Nippon Rinsho; 39(5):56-64 1981

Names and classification of hereditary cancer of the large intestine, types of hereditary gastrointestinal polyposis, types of non-polyposis hereditary cancer of the large intestine, the proportion of cancers of the large intestine which are due to genetic factors, clinical distinctions and diagnosis of hereditary cancer of the large intestine, biological markers of hereditary cancer of the large intestine, and countermeasures for hereditary cancer of the large intestine were discussed. Cancers of the large intestine that are observed in family medical histories were divided into hereditary or non-hereditary types. Included in the hereditary types were hereditary gastrointestinal polyposis (adenomas of the large intestine, Peutz-Jeghers syndrome, juvenile polyposis) and non-polyposis hereditary cancer of the large intestine (non-polyposis familial cancer of the large intestine, Muir-Torre syndrome). Of 241 patients who had rectal or transverse colon cancer, 11 (4.6%) had at least one family member (parent, sibling) who had also had cancer of the large intestine; statistically, hereditary factors were thought to be involved in at least one-half of these cases. Patients with hereditary large intestine cancer had a slightly higher av age than those with adenoma and slightly lower age than those with non-hereditary cancer of the large intestine. Hereditary cancers occurred more often on the right side of the large bowel than did non-hereditary cancer. Biomarkers for hereditary cancer of the large intestine were thought to be more definitively established for patients with polyposis than for those without polyposis. (43 Refs) (In JPN)

49. TWO FAMILIES WITH CANCER FAMILY SYNDROME.

Bulow S, Svendson LB, Shannon Danes B
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2716-2718 1981

Cancer family syndrome (CFS) in two families is reported. One family had 30 members in 4 generations, and reliable information is available on 29 members. Cancer was found in 11/29 cases (4 men and 7 women, age at the manifestation of the first cancer 33-38 yr, av 56 yr). The tumors included four colorectal carcinomas, four solitary colorectal adenomas, one skin cancer, two breast cancers, one gastric cancer, and one cancer of uterine cervix. Two primary cancers were found in one patient. Increased tetraploidy of skin fibroblasts, investigated in 13/29 cases, was found in 6/13 family members, 2 of whom were affected by cancer. The other family included 25 members in 4 generations; reliable information is available for 23 family members. Six members of this family, including three men and three women, had cancer: nine colorectal cancers and one retroperitoneal malignant tumor were diagnosed. There were 10 primary malignant tumors. The age of the patients at the time of manifestation of the first tumor was 37-51 yr (av 41 yr). Increased tetraploidy of skin fibroblasts, investigated in 10 family members, was found in 5/10 cases, including in 2 cancer patients. (8 Refs) (In DAN)

50. CANCER FAMILY SYNDROME.

Svendsen LB, Bulow S
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2713-2716 1981

Studies on cancer family syndrome (CFS) are reviewed. CFS is characterized by high frequency of adenocarcinoma, particularly in the colon and endometrium, high frequency of multiple synchronous cancer, early development of cancer, and autosomal dominant heredity. The risk of metachronous cancer is estimated at 3%/yr of survival after the first cancer and at 6.9%/yr of survival after the second cancer. The prognosis of cancer in CFS is relatively good, which may be due partly to awareness and resulting early detection. The variants of CFS include hereditary proximal colonic cancer, hereditary solitary colonic polyp, and recessive polyposis. (30 Refs) (In DAN)

51. QUESTIONS CONCERNING THE CANCEROUS TRANSFORMATION OF ULCERATIVE COLITIS AND CROHN'S DISEASE.

Muto T, Konishi F, Kamiya J
First Dept. Surgery, Tokyo Univ. Sch. Medicine, Tokyo, Japan
Nippon Rinsho; 39(5):71-76 1981

Because cases of cancer combined with ulcerative colitis or Crohn's disease are rare in the Japanese literature, relationships between cancer of the large intestine and ulcerative colitis and Crohn's disease were discussed with respect to literature from the West. Of 13,987 cases of ulcerative colitis reported from 1929-1961, 563 (3.1%) were observed to be accompanied by carcinoma; combined with histological findings, a relationship between ulcerative colitis and cancer was suspected. Distinctive features of cancer associated with ulcerative colitis included a flat tumor, irregular border between the cancer and the surrounding tissue, and a high frequency of poorly differentiated carcinoma and mucin-producing carcinoma. Patients with cancer and ulcerative colitis also tended to be younger than those with cancer of the large intestine only. Patients with Crohn's disease were also thought to have a high risk of cancer, although the number of patients with cancer of the large intestine and Crohn's disease was thought to be quite small. Diagnosis of early stage large intestine cancer and precancerous conditions was thought advisable in Japan as increasing frequency of ulcerative colitis and Crohn's disease in Western countries would probably be observed in Japan in the future as well. (44 Refs) (In JPN)

52. NON-POLYPOSIS CANCER OF THE LARGE INTESTINE.

Oohara T, Ihara O
Third Dept. Surgery, Tokyo Univ. Sch. Medicine, Tokyo, Japan
Nippon Rinsho; 39(5):60-65 1981

Risk factors for large intestine cancer were investigated by examining the intestinal mucosa of 495 patients (278 men, 217 women; 19-90 yr old) who had non-polyposis intestinal cancer. The potential for intestinal adenoma to be a site for large intestinal cancer to occur was thought to be high, but discovery was difficult owing to the small size of the lesions; 12.5% of the cases of intestinal cancer had microscopic adenomas in the mucosa surrounding the cancer which were not macroscopically observable. The cancers were thought to occur due to adenomatous changes in the basal cells of the microscopic adenomas, and 38.4-62.6% of the adenomas were observed to have such changes occurring. Residual adenoma tissues were observed in 6.7% of the advanced cancers of the large intestine. Risk of cancerous change was thought to be high even in nonpolyposis large intestines if the intestinal mucosa had microscopic adenomas and the basal cells showed adenomatous changes. (20 Refs) (In JPN)

53. POLYPS AND COLORECTAL CANCER IN SOUTH AFRICAN BLACKS.

Segal I, Cooke SA, Hamilton DG, Tim LO
Gastroenterology Unit, Baragwanath Hosp., P. O. Berstham 2013, Johannesburg, South Africa
Gut; 22(8):653-657 1981

This study reflects the fact that cancer of the large bowel is uncommon in South African blacks, and that colorectal polyps do not appear to constitute a precursor to most colorectal cancers. Furthermore, it is shown that dietary factors associated with this cancer in western populations are not evident in the black population. In the South African white population, however, the disease behaves in a similar way to that observed in western countries. Other definitive differences found were the absence of multiple synchronous cancers and diverticular disease in the blacks with colorectal cancer. It is thus postulated that dietary factors are absent, or have not been present for a sufficient length of time to influence the development of polyps or polyp-cancer sequence in this population. It is also possible that the adenoma-carcinoma progression observed in Western countries may not be relevant to the development of all colorectal carcinomas in communities such as those reported here. (Author abstract) (19 Refs)

54. PATIENTS WITH GASTRIC POLYPS: A RISK GROUP FOR COLORECTAL TUMORS? HEMOCCULT TESTS ON 106 PATIENTS.

Liebe S, Wohlgemuth B
Medizinische Universitatsklinik der Karl-Marx-Univ., Johannisallee 32, DDR-7010 Leipzig, E. Germany
Z Gesamte Inn Med; 36(18):682-684 1981

Hemoccult tests (HOT) were performed on feces from 106 patients who had previously had gastric polyps (GP) removed. Adenoma of the colon had been removed from 11 of these patients before examination. HOT detected two additional carcinomas and two adenomas of the colon, as well as two recurrences of previously treated adenomas. The occurrence of colorectal tumors (CRT) in 15/106 patients indicates that patients with GP are a high-risk group for CRT and should be closely monitored. (9 Refs) (In GER)

55. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.

Kalmaz EV, Kalmaz GD
Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
Chemosphere; 10(10):1163-1175 1981

Effects of chlorine residuals and organic compounds in drinking water and aquatic environments, particularly direct toxicity and/or carcinogenicity to human and aquatic life, are reviewed. Significant correlations between surface water chlorination and cancer mortality rates have been shown in humans. Elevated rates of bladder, rectal, colon, and gastrointestinal cancers in humans served by chlorinated water from the Mississippi River have been demonstrated. The use of chlorinated surface waters in Ohio was associated with stomach cancer in males and females, and with bladder cancer in males. Chloramine has been shown to be an extremely weak mutagen; involvement of DNA is suggested, since DNA-repair mutants are sensitive to the agent. In uremic patients, shortened RBC survival and hemolysis have been attributed to chlorinated tap water used in hemodialysis. Effects on aquatic life of chlorine residuals are reviewed. While more than 300 chlorinated organic compounds have been identified in chlorinated potable waters, cooling waters, and sanitary effluents, relatively little is known about their ecological effects. Laboratory research using animal models should focus on the chloramines and their effects on health. (65 Refs)

56. RETHINKING THE ENVIRONMENTAL CAUSATION OF HUMAN CANCER.

Higginson J
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Food Cosmet Toxicol; 19(5):539-548 1981

Epidemiologic studies concerning the etiology of environmental cancers are reviewed. The results of a number of studies strongly suggest that most human cancers are related to environmental factors and not to racial or hereditary factors. The results of the author's survey in South Africa further suggested that 'way of life' was of major significance for many cancers, especially those of the gastrointestinal tract and endocrine-dependent organs. Although there are many factors involved in its etiology, cancer may be prevented by controlling a single predominant factor. Only a small part of the total cancer burden can be directly related to ambient environmental pollution, and a number of other environmental factors, particularly diet, must be considered for the majority of environmental cancers. Although the role of dietary factors in promotion and enzyme induction of cancers is well established in laboratory animals, their role in man is much less clear. Most epidemiologists do not consider human environmental cancers in terms of single causes; human cancers for which there is evidence of multistage and multifactorial origin include lung, esophagus, liver, stomach and large intestine, breast and endometrium, Burkitt's lymphoma, and nasopharyngeal carcinoma. (106 Refs)

57. CHEMICAL AND ENVIRONMENTAL AGENTS IN GASTROINTESTINAL CARCINOGENESIS.

Deschner EE, De Cosse JJ, Sherlock P
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Clin Gastroenterol; 10(3):755-771 1981

A review is presented of incidence, risk factors, and chemical and environmental agents involved in induction or promotion of cancer of the gastrointestinal system. Presence of ingested agents in foods and experimental and clinical evidence for cancer causation are discussed. Carcinogenesis is considered with respect to the esophagus (nitrosamines, mycotoxins, promotional factors), stomach (nitrites and polycyclic hydrocarbons, mycotoxins, agricultural products, polychlorinated biphenyls, experimental carcinogens), and large bowel (nitrites, aflatoxins, diet, carrageenan, chemical carcinogens: nitroso compounds, biphenyls, symmetrical 1,2-dialkylhydrazines and azoalkanes and azoxyalkanes). Chemicals with known gastric tumor induction capability in animals are tabulated from published reports. (74 Refs)

58. HOW HIGH A PERCENTAGE OF ENVIRONMENTALLY RELATED CANCER CASES CAN BE PREVENTED IN NORWAY?.

Langard S
Yrkesmedisinsk avdeling, Telemark sentralsjukehus, 3900 Porsgrunn, Norway
Tidsskr Nor Laegeforen; 101(28):1602-1606 1981

Approx 110,000 cases of cancer were recorded in Norway during the period 1966-1975. Esophageal cancer was diagnosed in 1.099 cases, gastric cancer in 11,702, cancer of the gastrointestinal tract in 9,270, rectal cancer in 4,670, cancer of the liver and bile ducts in 253, pancreatic cancer in 3,992, larynx cancer in 745, lung cancer in 7,608, prostate cancer in 10,835, renal cancer in 3,191, cancer of the bladder and urinary tract in 4,047, and malignant lymphoma in 3,336. The percentage of environmentally related, ie, preventable cancer was estimated after extrapolation to the 1979 incidence. According to the low estimate, 2,250 cases of cancer were attributable to smoking, 300 to alcohol consumption, and 150 to occupational exposure. (15 Refs) (In NOR)

59. MALIGNANT GASTRO-INTESTINAL TUMOURS. THE FREQUENCY DISTRIBUTION BY AGE, SEX, RACE AND SITE AT GROOTE SCHUUR HOSPITAL, CAPE TOWN, 1974-1978.

Dent DM, Vader CG
Dept. Surgery, Groote Schuur Hosp., Cape Town, South Africa
S Afr Med J; 60(23):883-885 1981

The observed frequency distribution of 2,023 primary malignant gastro-intestinal tumors recorded during the 5-yr period 1974-1978 is reported. The two most common sites were stomach (29.6%) and colon and rectum (29.5%), and the third most common was the esophagus (19.8%). Marked differences in the site of the tumors according to race were found; esophageal carcinoma was the most frequent lesion in Black patients (62.1%), gastric carcinoma in Colored patients (44.1%) and colorectal carcinoma in White patients (46.8%). Within the Black group rarely affected sites were the pancreas (5.1%) and colon and rectum (3.5%). (Author abstract) (6 Refs)

60. EPIDEMIOLOGICAL VICISSITUDES OF LARGE INTESTINE CANCER AND OUTLOOK FOR THE FUTURE.

Hirayama T
Dept. Epidemiology, Natl. Cancer Res. Center, Tokyo, Japan
Nippon Rinsho; 39(5):10-20 1981

Age-adjusted death rates for transverse colon cancer and rectal cancer increased from 1950-1978 in Japan. In 1950 and 1978, respectively, death rates (per 100,000 population) for transverse colon cancer were 1.7 and 3.8 for men and were 2.2 and 4.1 for women; those for rectal cancer were 2.8 and 3.8 for men and 2.5 and 3.0 for women, respectively. Analysis of annual transitions of death rates by age groupings showed that death rates due to transverse colon cancer increased from 1950-1978 in all age groups, and the trend was slightly higher for men than women; except for women 40-44 yr old, death rates due to rectal cancer remained the same or decreased slightly for both men and women. By region, both age-adjusted death rates and rates of chronic disease due to transverse colon cancer showed marked increases for both men and women, and rates of increase of chronic disease due to transverse colon cancer are now 2x those for lung cancer in both men and women. Autopsy studies from 1968-1978 showed that the incidence of cancers in the sigmoid flexure increased 3.1x in men and 2.6x in women. Cigarette smokers had high death rates due to large intestine cancer, and meat eaters had low rates of death due to large intestine cancer. Extrapolation of current data indicates that death rates due to large intestine cancer will continue to rise in the future. Preventative effects of fibrous foods need to be investigated as one aspect of research on changing this trend. (no Refs) (In JPN)

61. CHANGES IN JAPANESE EATING HABITS AND CANCER OF THE LARGE INTESTINE.

Narisawa T
First Dept. Surgery, Akita Univ. Sch. Medicine, Akita, Japan
Nippon Rinsho; 39(5):26-31 1981

Relationship between increasing rates of cancer of the large intestine and changes in eating habits by Japanese was studied with the aid of experimental animal models and review of literature. Epidemiological studies indicate that environmental and lifestyle differences account for increasing incidence of large intestine cancer more than genetic or anthropological factors. Data from experiments on producing cancer of the large intestine in rats fed either high protein (40%) and high fat (20%) diets or standard diets (20% protein, 5% fat) along with carcinogenic substances such as 1,2-dimethylhydrazine or azoxymethane supported epidemiological studies indicating that high fat and protein diets were related to high rates of cancer. Other studies on relationship of fiber content in the diet and cancer of the large intestine suggested that prolonged retention of fecal matter in the intestinal lumen increased the concentration and carcinogenic potential of secondary bile acids in fecal matter. Japanese dietary intake of fats has increased 2.2x in the past 20 yr, and concurrent with a rise in consumption of meat (50% of protein intake), the fats consumed are increasingly from animal sources instead of vegetable sources. With decreased consumption of grains, the fiber intake of Japanese had also diminished, reducing the amount of fecal matter and increasing the concentration of bile acids. (32 Refs) (In JPN)

62. NUTRITION AND CANCER: A REVIEW.

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Praxis; 70(43):1903-1912 1981

The possible roles of various nutrients in carcinogenesis are reviewed. Epidemio logical studies indicate a high rate of carcinomas of the breast (BC) and colon (CC) in industrialized countries. Dietary factors are suggested by changes in cancer frequencies among immigrant populations and their descendants. Dietary studies indicate a positive correlation between dietary fat and CC and BC, as well as a negative correlation between these cancers and dietary fiber content. Animal studies have shown a cancer-promoting effect for fats, particularly unsaturated fats. Fats may promote cancer by affecting specific intestinal bacterial populations, bile secretion, hormonal balance, and immune response. Fiber may reduce cancer risk by speeding the movement of carcinogens through the digestive tract. Cancer risk has not been confirmed for proteins or their pyrolysis products. Some studies have indicated risk associated with pickled, smoked, or fried foods related to production of nitrosamines and nitrosamides. These compounds, which have been shown to be carcinogenic, are formed in vitro from nitrites and secondary amines. Their formation appears to be limited by the presence of ascorbic acid or vitamin E. Further studies of dietary factors are indicated. (130 Refs) (In GER)

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Diagnosis, Treatment

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. SCREENING FOR CANCER OF THE COLON IN BORSOD COUNTY.

Ujszaszy L, Nagy Gy, Pronay G
II. Belgyogyaszati Osztalyt, Borsod-Abauj-Zemplen Megyei Korhaz-Rendelointezet, Miskolc, Hungary
Magy Onkol; 25(4):266-271 1981

The value of rectoscopy and of the Hemoccult test in screening for cancer of the colon was analyzed. Rectoscopic screening was performed on 7,158 symptom-free subjects above the age of 45 yr. The screening revealed rectosigmoid carcinoma in 2 patients and 121 polyps in 112 patients. Other 1,889 symptom-free subjects (above 45 yr) were submitted to screening by the Hemoccult test. The test results were positive in 101 cases: carcinoma of the colon was subsequently diagnosed in 4 patients, poly ps in 16, anal lesion or proctitis in 68, diverticulum in 4, duodenal ulcer in 2, and gastric cancer in 1. It was not possible to establish the source of the bleeding in six patients. The Hemoccult test was performed in 412 patients 1.5-12 (av 5.8) yr after polypectomy. The test results were

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positive in 46/412 patients: carcinoma of the colon was subsequently diagnosed in 3/46 patients, recurrent polyps in 14, and lesion or proctitis in 21, diverticulum in 3, and the source of bleeding was not found in 5 patients. The examination of 50/412 patients in whom the result of the Hemoccult test was negative revealed recurrent colonic polyps with diameters smaller than 0.5 cm in 7/50 cases. (22 Refs) (In HUN)

2. THE CLINICAL SIGNIFICANCE OF LARGE LYMPHOID FOLLICLES OF THE COLON.

Kenney PJ, Koehler RE, Shackelford GD
Dept. Radiology, Upstate Medical Center, Syracuse, NY, 13210
Radiology; 142(1):41-46 1982

In 17 patients, large colonic lymphoid follicles were visible on air-contrast barium-enema examination (ACBE). They varied in size but were at least 4 mm in diameter and located predominantly in the rectosigmoid region. Inflammatory bowel disease was found in 13 patients (73%) and lymphoma in 1. In 100 controls without signs or symptoms of inflammatory bowel disease, the lymphoid follicles did not exceed 3 mm; they were visible radiographically in 52% of patients under 30 and 17% of those over 30. Lymphoid follicles which measure greater than or equal to 4 mm on ACBE should suggest inflammatory bowel disease or, less likely, lymphoma or dysgammaglobulinemia. (Author abstract) (17 Refs)

3. A COMPARATIVE ULTRASTRUCTURAL STUDY OF HYPERPLASTIC AND ADENOMATOUS POLYPS, INCIDENTAL AND IN ASSOCIATION WITH COLORECTAL CANCER.

Mughal S, Filipe MI, Jass JR
Dept. Histopathology, Westminister Medical Sch., Udall St., London SW1P 2PP, England
Cancer; 48(12):2746-2755 1981

Adenomatous polyps of the colon were examined by light and electron microscopy in high risk patients having synchronous carcinoma and in low risk patients having incidental polyps only. There was no difference between these groups when polyp size, degree of dysplasia, and pattern of growth were correlated at light microscopic level. However, the groups differed ultrastructurally; the synchronous polyps showed atypical features, characterized in particular by abnormal secretory droplets and increased numbers of undifferentiated cells. Hyperplastic polyps were also included in the study and showed no atypia. Previously, adenomas from cases of familial polyposis coli have been shown to contain similar abnormal secretory droplets, and it is suggested that this ultrastructural change may be an important marker of early malignancy. Histochemistry and immunohistology may help to characterize the secretory material further. (Author abstract) (26 Refs)

4. PROGNOSTIC SIGNIFICANCE OF CEA IN COLORECTAL CANCER: A STATISTICAL STUDY.

Persijn JP, Hart AA
Ziekenhuis Amsterdam-Noord, NL-1031 XP Amsterdam, The Netherlands
J Clin Chem Clin Biochem; 19(11):1117-1123 1981

Pretreatment and serial posttreatment levels of carcinoembryonic antigen (CEA) were studied in the sera of 222 patients with colorectal cancer; 205 patients underwent surgery as the primary treatment. Posttreatment levels during the subsequent 6 yr were expressed in actuarial or cumulative plots in relation to tumor-free period, time of diagnosis of recurrence, and time of diagnosis in local and distant recurrences. While pretreatment levels of CEA were significantly elevated, they gave no more prognostic information than that provided by the Dukes classification. Tumor-free periods of Dukes B patients were not significantly different if grouped according to different levels of their pretreatment CEA values. Among 144 patients with pretreatment values greater than 4.9/liter, 20 had residual tumor; two of these patients had CEA values which decreased to less than 5.0/liter within 100 days despite residual tumor, suggesting the possibility of a 'false' decrease. Pretreatment CEA values only had prognostic value in inoperable patients. Elevated pretreatment CEA did not exclude the possibility of curative treatment. Normalization of CEA after surgery did not indicate completeness of cure. In patients with local or distant recurrences, CEA in some instances rose before recurrences became clinically apparent. In approx 40% of patients, clinical diagnosis of recurrence preceded a rise in CEA. Max negative lead time was 385 days. Recurrence without a rise in CEA was exceptional. Results strongly suggest that serial CEA determinations cannot replace physical examination and follow-up. (28 Refs)

5. PROGNOSTIC VALUE OF PREOPERATIVE SERUM CEA LEVEL COMPARED TO CLINICAL STAGING. I. COLORECTAL CARCINOMA.

Staab HJ, Anderer FA, Brummendorf T, Stumpf E, Fischer R
(c/o Anderer), Friedrich-Miescher-Laboratorium der Max-Planck-Gesellschaft, Spemannstrasse 37-39, 7400 Tubingen, W. Germany
Br J Cancer; 44(5):652-662 1981

In a clinical investigation of observed postoperative survival, 563 patients have been registered for primary surgical treatment of colorectal cancer since 1974. The potential prognostic factors examined within the first days of hospitalization for primary resection included age of the patients, operability, location of the tumor, tumor extension and the preoperative serum CEA level. Statistical treatment of the data revealed that each of the clinical parameters except tumor location covers ranges associated with highly significant differences in survival of the patients. The preoperative serum CEA level gave prognostic information in addition to operability of tumor extension. The prognostic significance of the preoperative CEA level was still evident when selected subgroups of patients with distinct resectability and tumor extension were examined. The results indicate that the preoperative serum CEA level is an independent prognostic parameter. (Author abstract) (18 Refs)

6. A RETROSPECTIVE STUDY OF SERIAL CEA DETERMINATIONS IN THE EARLY DETECTION OF RECURRENT COLORECTAL CANCER.

Wedell J, Zu Eissen PM, Luu TH, Fiedler R, Van Calker H, Koldowski P, Schlipkoter HW
Kreiskrankenhaus Herford, Schwarzenmoorstr. 70, Postfach 523, 4900 Herford, W. Germany
Dis Colon Rectum; 24(8):618-621 1981

In the past 5 yr, routine CEA determinations have been carried out on all patients after curative operation for colorectal carcinoma. These patients also underwent a clinical follow-up examination in the Oncology Outpatient Department. In 86 patients, recurrence of a tumor was confirmed. In 31 cases, a second-look operation was carried out. The CEA determinations were retrospectively analyzed in these patients and correlated with the time the recurrence of the tumor was diagnosed. These results show that of 86 patients only 15 (17.4%) had pathologic CEA values before clinical symptoms of tumor recurrence. In the patient group with local recurrence, only 11

(23.9%) of 46 patients had previously pathologically raised CEA values. Of 31 patients, 15 (48.4%) underwent curative resection after the second-look operation. At this time, 12 patients (38.7%) still had normal CEA values, whereas only three patients (9.7%) had pathologically raised CEA values. From these results, it was established that early diagnosis of tumor recurrence was very low. Therefore, one should not rely more on postoperative routine CEA determinations in the postoperative monitoring of patients following curative operations for colorectal carcinoma than on regular comprehensive followup examinations of these patients. (Author abstract) (16 Refs)

7. POSTOPERATIVE SCREENING OF PATIENTS WITH CARCINOMA OF THE COLON.

Beart RW, Metzger PP, O'Connell MJ, Schutt AJ
Mayo Clinic, Rochester, MN, 55905
Dis Colon Rectum; 24(8):585-588 1981

A prospective evaluation of 149 patients with Dukes' B2 or C colorectal carcinoma, including periodic history, physical examination, chest radiograph, liver function tests, complete blood count, carcinoembryonic antigen (CEA) radioimmunoassay, barium enema, and endoscopic studies, has been underway since 1976. Thirty-four patients have had recurrence. This study suggests that the history and CEA are the most sensitive noninvasive methods with which to detect recurrent tumors but are unlikely to indicate recurrence at a therapeutically advantageous stage. (Author abstract) (14 Refs)

8. AN UNLABELED ANTIBODY METHOD USING GLUCOSE OXIDASE-ANTIGLUCOSE OXIDASE COMPLEXES (GAG): A SENSITIVE ALTERNATIVE TO IMMUNOPEROXIDASE FOR THE DETECTION OF TISSUE ANTIGENS.

Clark CA, Downs EC, Primus FJ
Div. Experimental Pathology, Dept. Pathology, Univ. Kentucky Medical Center, Lexington, KY, 40536
J Histochem Cytochem; 30(1):27-34 1982

Immunoenzyme staining for tissue antigens using glucose oxidase as marker enzyme was compared with immunoperoxidase techniques. Both the indirect, conjugated antibody method and the unlabeled antibody procedure employing preformed complexes of glucose oxidase-antiglucose oxidase (GAG) and peroxidase-antiperoxidase (PAP) were used to stain carcinoembryonic antigen (CEA) in paraffin tissue sections. The localization of CEA within a tissue specimen was the same in all cases, and background staining was minimal. The percentage of positive specimens detected with GAG and PAP was similar but was slightly greater with glucose oxidase compared to peroxidase conjugates. The glucose oxidase conjugates and GAG were similar to the comparable immunoperoxidase reagents in enzyme-antibody molar ratio, retention of antibody and enzyme activity, immunohistochemical staining dilutions, and stability. Immunoglucose oxidase and immunoperoxidase were combined to localize CEA and colon-specific antigen-p simultaneously. Excellent contrast and staining separation were shown between the enzymatic reaction products of the two systems. Since immunoglucose oxidase methods are as sensitive as the comparable immunoperoxidase techniques, they should be considered as a reliable alternative to the latter, especially when endogenous peroxidase activity may be a problem. Furthermore, the two methods can be conveniently combined for the simultaneous detection of two antigens. (Author abstract) (35 Refs)

9. VALUE OF PLASMA ALPHA-1-ACID GLYCOPROTEIN ASSAY IN THE DETECTION OF HUMAN COLORECTAL CANCER: COMPARISON WITH CARCINOEMBRYONIC ANTIGEN.

Chu CY, Lai LT, Pokala HP
Dept. Medicine, Wayne State Univ., Harper-Grace Hosp., 3990 John R., Detroit, MI, 48201
JNCI; 68(1):75-79 1982

Plasma specimens assessed for carcinoembryonic antigen (CEA) in the clinical laboratory for the detection of colorectal cancer were simultaneously assayed in our laboratory for alpha-1-acid glycoprotein (alpha1AG), by means of a solid-phase enzyme-linked immunosorbent assay we developed. In 28 patients with colorectal cancer of Dukes A, B, and C classes, elevated levels of alpha1AG were seen in 12 and of CEA in 8. In 44 patients with distant metastasis (Dukes D lesions), elevated plasma levels of alpha1AG were seen in 29 and of CEA in 34. No statistical differences in the detection rate were found among these markers in these two groups of patients. In 33 cases of non-neoplastic disease involving the large bowel, elevated plasma levels of alpha1AG were seen in 6, and elevated CEA levels were seen in 7. There was no statistical difference of false positive rates among these two markers. Elevated plasma levels of either CEA or alpha1AG were found in 57 cases of colorectal cancer. This preliminary study suggests that the sensitivity of the plasma alpha1AG assay is similar to that of the CEA assay in the detection of colorectal cancer. The combination of these two assays increases the detection rate of colorectal cancer significantly. (Author abstract) (32 Refs)

10. 3. MARKERS OF MINIMAL RESIDUAL DISEASE.

Neville AM
Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sotton, Surrey SM2 5PX, England
Recent Results Cancer Res; 80:17-21 1982

Current methods employing tumor markers to detect small amounts of residual disease are reviewed with respect to human germ cell, colorectal and breast neoplasms. It is concluded that the assay of tumor markers in body fluids has only limited clinical value. Alternative approaches, such as are afforded by radioimmunodetection and immunocytochemistry, are presented and critically appraised. (Author abstract) (15 Refs)

11. CONCOMITANT HEPATIC RADIATION AND INTRAARTERIAL FLUORINATED PYRIMIDINE THERAPY: CORRELATION OF LIVER SCAN, LIVER FUNCTION TESTS, AND PLASMA CEA WITH TUMOR RESPONSE.

Lokich J, Kinsella T, Perri J, Malcolm A, Clouse M
Dept. Medicine, New England Deaconess Hosp., 185 Pilgrim Road, Boston, MA, 02215
Cancer; 48(12):2569-2574 1981

Sixteen patients with metastatic disease to the liver (12 colorectal and 4 unknown primary tumors) were treated in a pilot study of hepatic irradiation (2,500-3,000 rads in 10-12 fractions) delivered concomitantly with continuous short-term intraarterial infusion of 5-fluorouracil (1 g/d) or FUDR (0.5 mg/kg/d) via a percutaneously placed hepatic artery catheter. Abnormal liver function tests, including SGOT, LDH, and alkaline phosphatase, decreased in all patients by day 7-10 of treatment, and other metabolic factors, including serum cholesterol, calcium, albumin, phosphorous, and uric acid, also decreased, often to subnormal levels by termination of treatment (day 15-20). These chemical alterations did not correlate with tumor response in that the identical pattern was observed in responders (10 patients) as well as nonresponders (6 patients). Objective determinants of response were assessed by serial monitoring of plasma carcinoembryonic antigen (CEA) and liver scan. In 14 patients with elevated CEA levels, tumor response (9 patients), nonresponse (4 patients), and relapse (5 patients) was predicted and confirmed by sequential monitoring of CEA. In one patient, a paradoxical decrease in plasma CEA was associated with progressive disease. The liver scan identified all responding patients but was difficult to quantitate and was delayed for months following subjective clinical response and changes in plasma CEA levels. (Author abstract) (17 Refs)

12. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY IN HUMAN CANCER: CHARACTERIZATION OF PATIENT LEUKOCYTE ACTIVITY AND TREATMENT EFFECTS.

Hersh EM, Murphy SG, Gutterman JU, Morgan J, Quesada J, Zander A, Stewart D

M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030

Cancer; 49(2):251-260 1982

Antibody-dependent cell-mediated cytotoxicity (ADCC), mediated by peripheral blood Hypaque-Ficoll separated mononuclear cells, was studied in humans using chicken erythrocytes (CRBC) incubated in a 1:1,200 dilution of rabbit anti-CRBC and human B erythrocytes (HRBC) incubated in a 1:20 dilution of isoantibody. At the optimal target effector ratio of 3:1, ADCC to both CRBC and HRBC was significantly higher than normal in 27 lung cancer, 18 malignant melanoma, and 7 colon cancer patients, but not in 20 breast cancer patients. Chemotherapy (single-agent or combination) in 12 patients did not affect ADCC in vitro but significantly suppressed ADCC to both targets after only 4 or 5 days of therapy in vivo (ADCC to CRBC, 47.4 to 24.1% lysis: ADCC to HRBC, 48.1 to 16.3% lysis). Immunotherapy with intravenous (IV) Corynebacterium parvum or IV methanol extraction residue of BCG (MER) boosted ADCC to both targets within 4 to 7 days of the first dose. It was found that ADCC to HRBC but not to CRBC was completely absent in three cases of active hairy cell leukemia but was present in two cases in remission. The ADCC to HRBC showed an age-dependent increase in both the 51 normal subject and the cancer patients. This was not observed for ADCC to CRBC. The ADCC to CRBC was mediated mainly by an Fc-receptor-positive, nonadherent, small lymphocyte, and ADCC to HRBC was mediated entirely by an adherent monocyte. The ADCC did not correlate significantly with the H3 thymidine incorporation of peripheral blood mononuclear cells, cultured without stimulation for either 1 or 7 days. It also did not correlate with the number of residual granulocytes in the mononuclear cell suspensions. Measurement of ADCC is a useful method of characterizing host defense in malignant disease and its modification by therapy. (Author abstract) (48 Refs)

13. STUDIES ON CELL-MEDIATED IMMUNITY IN PATIENTS WITH COLORECTAL CANCER: LEUKOCYTE MIGRATION INHIBITION TEST (LMIT) USING ALLOGENEIC 3 M KCL EXTRACTS.

Kitagawa N

First Dept. Surgery, Kyoto Prefectural Univ. Medicine, Kamigyo-ku, Kyoto 606, Japan

Kyoto Furitsu Ika Daigaku Zasshi: 90(6):473-483 1981

The cellular immune response to tumor-associated antigens (TAA) had been monitored in patients with malignant tumors. In the present study, WBC from patients with colorectal and other malignant and nonmalignant gastrointestinal diseases and from normal subjects were tested by the LMIT, utilizing five different allogeneic 3 M KCl soluble extracts of colorectal cancer tissues. The normal ran ge of the migration index (MI) was found to be 0.82 to 1.20 by calculating the mean MI +-2 SD (standard deviation) of 10 normal subjects. MIs out of this range were considered to be pathologic. In the LMIT with a single tumor extract, pathologic MI was found in 49.3% of 71 colorectal cancer patients, significantly higher than the 12-15% of other patients. In the panel method, ie testing each blood sample with five different tumor extracts, 78.9% of the patients with colorectal cancer were reactive, while 15% of gastric cancer patients showed positive reactions and no reactivity was observed in another group of patients. The difference between the colorectal cancer patients and the other patients was statistically significant. The frequency of positive reactivity was not related to the carcinoembryonic antigen value in the extracts. Markedly depressed reactivity was seen 10-14 days after curative resection, and in patients without recurrence the MI was normal during the 1-2 mo after surgery. However, positive reactions recurred in patients with local recurrence. Thus, the LMIT, particularly when tested by a panel method, seems to detect cell-mediated immunity against TAA of colorectal cancer. (28 Refs) (In JPN)

THERAPEUTIC MODES OF COLO-RECTAL TREATMENT

14. COMPARATIVE RESULTS OF SURGICAL MANAGEMENT OF SINGLE CARCINOMAS OF THE COLON AND RECTUM: A SERIES OF 1939 PATIENTS MANAGED BY ONE SURGEON.

McDermott FT, Hughes ES, Pihl E, Milne BJ, Price AB

Dept. Surgery, Monash Univ., Alfred Hosp., Prahran, Victoria 3181, Australia

Br J Surg; 68(12):850-855 1981

A comparative analysis has been made of the results of surgical management of single carcinomas of the colon and rectum in a series of 1,939 patients treated by one surgeon. The data were prospectively collected, with 99% follow-up. Cancer specific survival did not differ significantly between patients with colonic or rectal cancer. Survival prospects were better for women (p = 0.02) and for patients less than 40 yr of age (p = 0.03). Survival was significantly related to tumor staging (p less than 0.001). Cancer specific survival was better after curative resection for colonic than rectal carcinoma (p = 0.003). Five-yr survival for patients with colonic tumors was 76% and for rectal tumors 69%. The 10-yr survival figures were 73% and 61% respectively. This difference was accounted for by a higher proportion of dukes' Stage C tumors in the rectum (p less than 0.001) and better survival prospects for colonic compared to rectal Stage C1 tumors (p = 0.02). Sphincter-saving resections were performed in 64% of rectal cancer patients managed by curative resection. Survival tended to be better than after sphincter-sacrificing operations. After palliative resection, median survival for colonic and rectal cancer was 14 and 13 mo respectively. After palliative bypass operations the corresponding figures were 4 and 8 mo. (Author abstract) (35 Refs)

15. TOTAL PELVIC EXENTERATION IN COLORECTAL DISEASE. A 20-YEAR EXPERIENCE.

Ledesma EJ, Bruno S, Mittelman A
Dept. Health, State of New York Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Ann Surg; 194(6):701-703 1981

Between 1955 and 1975, 30 patients (7 men, 23 women; 43-83 yr old) underwent total pelvic exenteration for locally extensive colorectal adenocarcinoma. Postoperative mortality was 10%. The 5-yr survival was 43%. (6 Refs)

16. BASAL CELL CARCINOMA OF THE ANUS - A CLINICAL STUDY OF 34 CASES.

Nielsen OV, Jensen SL
(c/o Jensen) Dept. Surgical Gastroenterology C, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen O, Denmark
Br J Surg; 68(12):856-857 1981

Thirty-four patients with basal cell carcinoma of the anus were treated in Denmark between 1943 and 1974. The tumors were usually between 1 and 2 cm in diameter and localized to the anal margins. Three tumors had a diameter of 10 cm and extended into the anal canal. In one case the tumor had spread to the regional lymph nodes. Modes of treatment were wide local excision (27 patients), abdominoperineal excision of the rectum (4 patients), colostomy combined with radiotherapy (1 patient) and radiotherapy alone (2 patients). Local recurrence was observed in eight cases. After retreatment (re-excision: 5 patients), excision of the rectum (1 patient) and radiotherapy (2 patients), no recurrences were observed in the follow-up period (greater than 5 yr). The crude 5-yr survival rate was 72.6%. The death rate was not higher than in the normal population of the same age and sex and no death was due to the basal cell carcinoma. (Author abstract) (9 Refs)

17. A PROSPECTIVE STUDY OF BLADDER FUNCTION BEFORE AND AFTER SPHINCTER-SAVING RESECTIONS FOR LOW CARCINOMA OF THE RECTUM.

Neal DE, Williams NS, Johnston D
Univ. Dept. Surgery, General Infirmary, Leeds LS1 3EX, England
Br J Urol; 53(6):558-564 1981

The effects of sphincter-saving resections for carcinoma of the rectum on bladder function were studied prospectively. Twenty-seven patients, each acting as his or her own control, were studied before, shortly after and 9 mo after operation by means of pressure/flow filling and voiding cystometry. After operation there was a significant and lasting increase in the residual volume of urine and a temporary decrease in the compliance of the bladder. There was a statistically significant decrease in detrusor contraction pressure after operation, which persisted throughout the period of study. This was probably due to partial denervation of the bladder. Four patients had signs of total or almost total denervation of the bladder. There was a significant correlation between proximity of the tumor to the anal verge and risk of damage to the nerve supply to the bladder. Thus sphincter-saving resections of the rectum for carcinoma are associated with a significant risk of bladder denervation. Many of the 'minor' symptoms of bladder dysfunction which develop after this procedure are due to partial denervation of the bladder. (Author abstract) (29 Refs)

18. GIANT PSEUDOPOLYPS IN CROHN'S COLITIS: A NONOPERATIVE APPROACH.

Katz S, Rosenberg RF, Katzka I
1300 Union Turnpike, New Hyde Park, NY, 11040
Am J Gastroenterol; 76(3):267-271 1981

Six patients with Crohn's disease and colonic intraluminal multilobulated masses detected on barium enema. Four had Crohn's colitis and two ileocolitis. The mean duration of disease was four and eight tenths years. Three patients underwent surgery and three had colonoscopy with multiple biopsies and cytology. Pseudopolypoid inflammatory tissue was found in each case. One patient died after a prolonged postoperative course due to sepsis and abscess formation. No surgery was performed in three patients and follow-up colonoscopic examinations at four and a half years revealed no change in these findings. The presence of an intraluminal colonic mass in Crohn's colitis may mimic a neoplasm. If surveillance with x-ray, endoscopic biopsies and cytology reveals pseudopolypoid inflammatory tissue then surgery is not mandatory. Pseudopolypoid inflammatory tissue has never been associated with carcinoma. (Author abstract) (29 Refs)

19. ENDOSCOPIC POLYPECTOMY: INADEQUATE TREATMENT FOR INVASIVE COLORECTAL CARCINOMA.

Colacchio TA, Forde KA, Scantlebury VP
Dept. Surgery, Coll. Physicians and Surgeons, Columbia Univ., 630 W. 168th St., New York, NY, 10032
Ann Surg; 194(6):704-707 1981

Endoscopic polypectomy has greatly decreased the necessity for transabdominal resection of adenomatous polyps of the colon and rectum. In addition, the routine removal of these presumed precancerous lesions may well decrease the incidence of colon cancer in these patients. However, some authors have proposed that endoscopic resection alone of certain pedunculated polyps containing invasive carcinoma is adequate treatment for these lesions. At Columbia-Presbyterian Medical Center this has not been our standard practice, and 729 patients who have undergone endoscopic removal of pedunculated adenomatous polyps of the colon and rectum during the past decade have been reviewed. Forty-seven (6.4%) of these patients had polyps containing carcinoma in situ for which no further resection was performed. Thirty-nine patients (5.3%) had polyps containing carcinoma which had invaded up to or through the muscularis mucosae and were, therefore, considered invasive carcinomas. In this latter group, 24 patients underwent colon resection and 15 underwent endoscopic polypectomy alone. Within the group undergoing resection, six patients (25%) had from one to two lymph nodes within the resected specimen containing metastatic cancer. In review of these lesions, all 24 were able to be resected with an intervening segment of uninvolved stalk. After analyzing the frequently quoted parameters of size, depth of invasion into the stalk, degree of differentiation and involvement of lymphatics within the polyp, it was not possible to predict which lesions would have lymph node metastases at the time of resection. Consequently, it is concluded that all patients with polyps containing invasive carcinoma should undergo standard colon resection if feasible, despite the technical ability to resect these lesions endoscopically with an 'adequate' margin of uninvolved stalk. This will eliminate the possibility of undiagnosed Dukes' Stage C lesions, and potentially improve long-term survival rates within this group of patients with an otherwise poor prognosis. (Author abstract) (15 Refs)

20. HEPATIC RESECTION OF METASTATIC COLORECTAL CARCINOMA. A TEN-YEAR EXPERIENCE.

Logan SE, Meier SJ, Ramming KP, Morton DL, Longmire WP
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Arch Surg; 117(1):25-28 1982

Nineteen patients have undergone partial hepatectomy for metastatic colorectal carcinoma at UCLA during the past 10 yr, including 5 trisegmentectomies (TS), 8 lobectomies (L), and 6 segmentectomies (SG), with only 1 (5.3%) mortality. Twelve lesions were solitary (S) and 7 multiple (M). Mean survival is 27.4 mo, with three patients surviving over 5 yr and one nearly 8 yr. Better mean survival exists for S (33.2 mo) compared with M (15.8 mo) lesions; for lesser resections: SG (44.7 mo), compared with L (24.3 mo) and TS (11.0 mo); and for those with delayed appearance of hepatic metastases: beyond 2 yr (40.5 mo), less than 1 yr (24.8 mo), and synchronous (23.1 mo). Survival figures should improve, as none of the 12 surviving patients have evidence of recurrent disease and many have short follow-up. This experience defends aggressive surgical treatment of resectable colorectal carcinoma metastatic to liver, because systemic therapy is markedly less effective. (Author abstract) (28 Refs)

21. ADJUVANT THERAPY FOR LARGE BOWEL CANCER; UPDATE OF VETERANS ADMINISTRATION SURGICAL ONCOLOGY GROUP TRIALS.

Higgins GA, Donaldson RC, Humphrey EW, Rogers LS, Shields TW
Veterans Admin. Medical Center, 50 Irving St., N.W., Washington, D.C., 20422
Surg Clin North Am; 61(6):1311-1320 1981

Eight prospective randomized clinical trials are reviewed and the results reported. Treatment modalities included preoperative radiotherapy (PRT), 5-fluorouracil (FU), prolonged intermittent therapy (PIT), methyl-1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (M) trials, and chemo-immunotherapy (CI). In PRT Trial-1, all patients with lesions within reach of the sigmoidoscope were randomized for surgery alone or for PRT at a dosage of 2000 rads over a 2-wk period, with surgery carried out after completion of radiotherapy. Data indicated that addition of PRT affords substantial therapeutic benefit. In PRT Trial-2, only those patients having histologically proven rectal carcinoma at a level requiring abdominoperineal resection were included. A dosage of 175 rad for each of 18 treatments over a 24-day period was administered. Although follow-up data are not complete, evidence suggests benefit from the treatment. PIT and FU trials prolonged the survival rate of patients. Combined M and FU trials have not yet given any evidence of therapeutic benefit. CI has been tested only in a small trial for patients with proven palliative resection. In addition to M and FU, patients received BCG methanol extract residue at a dosage of 2 mg divided into five id injections. Survival decreased, possibly due to tumor enhancement by the immunostimulant. (6 Refs)

22. ADJUVANT CHEMOTHERAPY IN CANCER OF THE COLON AND RECTUM: DEMONSTRATION OF EFFECTIVENESS OF PROLONGED 5-FU CHEMOTHERAPY IN A PROSPECTIVELY CONTROLLED, RANDOMIZED TRIAL.

Grage TB, Moss SE
Dept. Surgery, Univ. Minnesota Hosp., Box 90 Mayo, Minneapolis, MN, 55455
Surg Clin North Am; 61(6):1321-1329 1981

In a prospectively randomized study the effect of adjuvant chemotherapy with 5-FU (5-fluorouracil) on survival and recurrence rates was analyzed in 319 evaluable patients with colorectal carcinoma who underwent either a curative or a palliative resection. In the treatment group the chemotherapy consisted of iv administration of 12 mg/kg daily of 5-FU for four consecutive days, then 6 mg/kg on alternate days to the point of toxicity or to a max of five doses, followed by 12 mg/kg weekly for one yr. Some degree of drug toxicity was seen in the majority of the patients treated; however, it was rarely severe and there have been no drug-related deaths. Analysis of the survival curves and disease-free interval curves reveal definite evidence of drug benefit in two unfavorable subgroups, namely patients with Dukes C carcinoma and patients with the neoplasm located in the rectum. In the chemotherapy group, in patients who were treated to toxicity (white blood cell count of less than 4000 per cu mm) the disease-free interval was significantly longer than in the non-leukopenic patients. In this Central Oncology Group trial, the addition of 5-FU to the surgical treatment of colorectal carcinoma provides a small but significant benefit in patients with colorectal cancer in certain unfavorable subgroups, namely patients with Dukes C tumors and patients with rectal carcinoma. (Author abstract) (20 Refs)

23. ADJUVANT CHEMOTHERAPY IN COLON AND GASTRIC CANCER.

Macdonald JS, Haller DG, Kisner DL
Div. Cancer Treatment, Cancer Therapy Evaluation Program, NCI, Bethesda, MD, 202 05
Recent Results Cancer Res; 80:284-290 1982

The adjuvant chemotherapy of colorectal and gastric cancer is being actively investigated. Studies of both single antineoplastic agents and combinations of several drugs have been used. In colorectal cancer, single-agent therapy has not resulted in improved survival. Combination chemotherapy studies are at too early a stage to be evaluated. In gastric cancer, single-agent chemotherapy has not been effective as adjunctive treatment to surgery. Combinations of active agents in gastric cancer hold promise as effective surgical adjuvant therapy. (Author abstract) (19 Refs)

24. CHEMOTHERAPY OF CARCINOMAS OF THE DIGESTIVE TRACT.

Gisselbrecht C, Belpomme D, Mignot L, Marty M, Mathe G, Boiron M
Unite d'oncologie Clinique, Hopital Saint-Louis, 2 Place du Docteur Fournier, F-75475 Paris Cedex, France
Recent Results Cancer Res; 80:296-302 1982

Adjuvant chemotherapy trials in gastric and colorectal carcinomas are reviewed and no clear benefit from such treatment could be observed. To improve existing chemotherapy regimens, several pilot studies were performed in 95 gastric cancer and 85 colorectal carcinoma patients. Response rate for gastric carcinomas using the mitomycin C plus adriamycin plus 5-fluorouracil (5-FU) (FAM) regimen was 40% and was not improved by the addition of nitrosoureas. In colorectal carcinomas none of the combinations used gave better results than 5-FU alone. Fourteen patients with esophageal carcinoma were treated with combination CDDP and the response rate was as high as 50%. (Author abstract) (14 Refs)

25. PHASE II STUDY OF DIBROMODULCITOL IN COLORECTAL, KIDNEY, AND OTHER CARCINOMAS.

Mischler NE, Tormey DC, Klotz J, Borden EC, Ramirez G, Banerjee TK, Carr RM, Zaentz SD, Graf J
Wisconsin Clinical Cancer Center, K4-Rm. 662, Clinical Science Center, 600 Highland Ave., Madison, WI, 53792
Cancer Clin Trials; 4(4):407-410 1981

In a Phase II Study dibromodulcitol (DBD), an alpha-omega dibrominated hexitol, was used to treat 99 previously treated patients with colon, rectal, kidney, and other tumors. Six patients were ineligible and 10 patients were nonevaluable for response. Aside from thrombocytopenia toxicity was moderate. Twenty-three patients had platelet nadirs of less than 50,000/mm3 and there were three thrombocytopenic-associated drug deaths. One of 21 rectal and 1 of 13 kidney cancer patients entered a remission. All but seven patients had received previous treatment with one or more cytotoxic agents. Previously treated patients with colorectal and kidney cancer appear to be resistant to DBD. (Author abstract) (11 Refs)

26. EVALUATION OF BETA-2'-DEOXYTHIOGUANOSINE COMBINED WITH METHYL-CCNU OR MITOMYCIN IN ADVANCED COLORECTAL CANCER: A SOUTHWEST ONCOLOGY GROUP STUDY.

Gagliano RG, Panettiere FJ, Haas CD, Baker L, Hewlett J, Stuckey WJ, O'Bryan RM, Bottomley R, Heilburn LK
Southwest Oncology Group, Operations Office, 3500 Rainbow Blvd., Suite 100, Kansas City, KS, 66103
Cancer Clin Trials; 4(4):401-405 1981

Two hundred twenty eligible patients with metastatic colorectal carcinoma were treated with a combination of beta-2'-deoxythioguanosine (BTG), plus methyl-CCNU or mitomycin. There was no significant difference in overall response (CR/PR + stable) among fully evaluable patients between the mitomycin plus BTG arm 19/96 (19.7%) and the MeCCNU arm 26/87 (29.8%). Median survival of eligible patients was 19 wk with mitomycin plus BTG versus 21 wk with MeCCNU plus BTG: no difference. Median survival of responders (40 wk) and patients with stable disease (35 wk) was significantly better than patients with increasing disease (17 wk): p + 0.001. (Author abstract) (28 Refs)

27. METHYL-GAG IN PATIENTS WITH MALIGNANT NEOPLASMS: A PHASE I REEVALUATION.

Hart RD, Ohnuma T, Holland JF, Bruckner H
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Cancer Treat Rep; 66(1):65-71 1982

Methyl-GAG was given to 71 patients with advanced malignancies as a weekly brief infusion (30-120 min) or as a biweekly 24-or 120-hr infusion. Mucositis (stomatitis, pharyngitis, esophagitis, and, rarely, inflammation of other mucous membranes) was dose-limiting in all three schedules. Generalized fatigue, malaise, myalgia, dysesthesias, nausea, and vomiting were more frequent in the brief-infusion schedule. Myelosuppression was mild and not dose-related. Fever, ventricular arrhythmias, skin rash, tender swelling of the palms, neuropathy, and paralytic ileus were rare. Toxicity was increased in patients with renal insufficiency or 'third-space' fluid but was not increased by hepatic dysfunction. Cumulative and overlapping toxicity was evident only in the weekly schedule. Higher doses of methyl-GAG were tolerated when the duration of infusion was increased. The recommended doses for Phase II trials are 700 mg/m2 weekly as a 1-2 hr infusion, 850 mg/m2/24 hr biweekly, and 1,500 mg/m2/120 hr biweekly. Therapeutic effects were seen in all schedules and included objective responses in colon carcinoma (1 of 13 patients), renal cell carcinoma (1 of 9), and Hodgkin's lymphoma (1 of 2) and objective improvements in esophageal carcinoma (1 of 3), endometrial carcinoma (2 of 2), and leiomyosarcoma (1 of 3). (Author abstract) (21 Refs)

28. PHASE II STUDY OF HIGH-DOSE INTERMITTENT CYCLOLEUCINE IN COLORECTAL MALIGNANCIES.

Dindogru A, Leichman LP, Cummings G, Baker LH
Dept. Oncology, Wayne State Univ., 3990 John R, Detroit, MI, 48201
Cancer Treat Rep; 66(1):203-204 1982

The results of a Stage II clinical trial of cycloleucine in 29 patients (13 men, 16 women; 25-82 yr old) with advanced colorectal neoplasms are reported. Cycloleucine was administered at a dose of 50 g/square meter, iv, every 3 wk. Side effects included nausea, CNS toxicity, and myelosuppression. No partial or complete remissions were obtained; three patients showed stabilization of the disease of 8, 24+, and 24+ wk. (5 Refs)

29. CLINICAL EVALUATION OF IMMUNOCHEMOTHERAPY WITH STREPTOCOCCAL PREPARATION 'OK-432' ON INOPERABLE ADVANCED CANCERS.

Nio Y, Nitta N, Tanaka A, Ichikawa T, Henmi K
Dept. Surgery, Ako Municipal Hosp., Nakasu, Kariya, Ako, Hyogo Prefecture 6[illegible]-02, Japan
Nippon Geka Hokan; 50(5):704-716 1981

Results of treating 54 patients with OK-432 (picibanil) in combination with antineoplastic chemotherapy for advanced, inoperable cancers were compared with those in 70 patients treated with chemotherapy without OK-432 and those in 61 patients who were not treated with chemotherapy or OK-432. The patients in the combination group had gastric (17 cases), colorectal (4), liver (7), pancreas (3), gall bladder (4), or lung (16) cancers, or cancerous peritonitis (3). The patients in the chemotherapy group had gastric (31), colorectal (3), liver (7), gall bladder (2), or lung (16) cancers. Patients were administered 0.2-0.5 IU of the OK-432 every day or qod initially, and were given 1-5 IU as maintanence doses. According to Karnofsky's criteria, effective treatment (I-A, I-B, or I-C) ratings were obtained in 4/63 evaluable patients in the chemotherapy group and in 11/52 evaluable patients in the combination group. Mean survival times for the non-chemotherapy group patients, the chemotherapy group patients, and the combination group patients were 2.2 mo, 4.2 mo, and 5.9 mo, respectively, and the 1-yr survival rates were 0%, 6.0%, and 18.0%, respectively. Improved clinical results and survival rates were thought to be possible with immunochemotherapy based on OK-432. (17 Refs) (In JPN)

30. PHASE III STUDY OF LENTINAN.

Furue H, Itoh I, Kimura T, Kondo T, Hattori T, Ogawa N, Taguchi T
Second Dept. Internal Medicine, Teikyo Univ., Sch. Medicine, Itabashi-ku, Tokyo 173, Japan
Gan To Kagaku Ryoho; 8(6):944-966 1981

To evaluate the clinical efficacy of lentinan, an immunopotentiating agent and purified polysaccharide (beta[1 leads to 3]glucan) extracted from Lentinus edodes (an edible Japanese mushroom), a randomized control study (envelop method) was performed on patients with advanced or recurrent gastric or colorectal cancer in 64 major institutions, comparing 'combination therapy with lentinan and chemotherapeutic agent' with 'chemotherapy alone' as a control. As control chemotherapy, the combined administration of mitomycin C and 5-fluorouracil (MF) or the single administration of tegafur (FT) was selected. Five hundred and twenty-three patients were entered in the study. There were 239 patients in the control chemotherapeutic group (control group) and 284 patients in the group given combination therapy with lentinan and chemotherapeutic agent (treated group). Three hundred and seventy-five of the 523 patients were eligible, and there were 168 patients in the control group and 207 patients in the treated group. The clinical efficacy of lentinan was evaluated by its antitumor effect, prolongation of life and improvement in host immune response. Compared with chemotherapy alone, statistically significantly higher incidence of antitumor effect and prolongation of life were observed with lentinan treatment. By both purified protein derivatives skin tests and increase in peripheral blood lymphocytes counts, a greater improvement in host immune response was observed with lentinan treatment, and improvement in the host immune response coincided with prolongation of life. In all of the 284 patients in the treated group, side effects, which were observed in 16 patients, seemed to be caused by combination therapy with lentinan and MF or FT. The incidence was similar to that in the Phase I and II studies, and all side effects were transitional and not very serious. These results suggest that lentinan would be of use for patients with gastrointestinal cancer as an immunopotentiator in combination with chemotherapeutic agents. (27 Refs) (In JPN)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

31. REVIEW OF COLORECTAL CANCER IN PATIENTS UNDER AGE 40 YEARS.

Safford KL, Spebar MJ, Rosenthal D
General Surgery Service, Darnall Army Hosp., Fort Hood, TX, 76541
Am J Surg; 142(6):767-769 1981

Brooke Army Medical Center Tumor Registry records from 1947 through 1980 were reviewed. One hundred forty of 819 patients with colorectal cancer were aged 40 or less. The 5 yr survival rate was 35% and the 10 yr survival rate 32%. The predominant presenting symptoms were bleeding, pain and change of bowel habits. The median duration of symptoms was 3 mo. There were no Dukes' A patients. The 5 and 10 yr survival rates in 19 Dukes' B patients were 67%. Thirty-three Dukes' C patients had 5 and 10 yr survival rates of 37 and 30%, respectively. In 42 Dukes' D patients, however, there were no 5 yr survivors, and the mean length of survival was only 10 mo. Our findings support previous surveys which have concluded that stage at the time of diagnosis, rather than symptoms, duration or patient age, is the most accurate prognostic factor. (Author abstract) (19 Refs)

32. CARCINOMA OF THE RIGHT COLON: A CHANGE IN CHARACTERISTIC CONFIGURATION?

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South Med J; 74(12):1436-1438 1981

Carcinoma of the colon occurring to the right of the middle colic vessels is usually described as morphologically and clinically distinctive from cancers occurring in the left colon. Cancers of the right colon are characterized as polypoid tumors that are discovered in the search for occult blood loss, whereas carcinomas of the left and sigmoid colon are described as scirrhous and often annular in configuration, giving rise to obstruction as the characteristic clinical presentation. A personal experience with constricting annular lesions of the right colon that were considered atypical has led to a review of the total experience in colonic resections for cancer (excluding abdominoperineal resections for carcinoma of the rectum) at one metropolitan university medical center. Of 152 colonic resections for cancer within a 39-mo interval, 57 resections were for cancer of the right colon and 95 for cancer of the left colon. One half of the cancers of the right colon were annular, whereas only one third of those of the left colon were so described by operative, pathologic, and radiologic criteria. Differences in clinical presentation of cancers of the right and left colon are probably attributable more to the form and function of the colon in each anatomic region than to any characteristic configuration of the tumor itself. (Author abstract) (9 Refs)

33. INCIDENCE OF HEPATIC METASTASES OF MALIGNANT TUMORS AS A FUNCTION OF AGE AND SEX.

Pejchl S, Pejchlova J, Chaloupka F

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Vnitr Lek; 27(11):1073-1077 1981

The possible relationship between the age and sex of the patients, on one hand, and the incidence of hepatic metastases of malignant tumors, on the other hand, was studied in 2,270 primary malignant tumors confirmed at autopsy in 2,203 patients (av age at death 67.2 yr). Eleven hundred and sixty-six tumors were found in men and 1,104 in women. Carcinomas accounted for 94% of all tumors. Seven hundred and eighty-five hepatic metastases were found. The incidence of hepatic metastases was 146/437 colorectal tumors, 144/453 gastric tumors, 123/321 tracheal tumors, 107/208 tumors of the gallbladder and bile ducts, 84/142 pancreatic tumors, 55/142 breast tumors, 26/118 ovarian and uterine tumors, 11/102 prostatic tumors, 25/107 renal tumors, and 84/249 miscellaneous tumors. At an overall metastasis frequency of 34.6%, the corresponding frequencies of hepatic metastases were 43.2% for patients 16-40 yr old, 38% for 41-50 yr old, 40.2% for 51-60 yr old, 35% for 61-70 yr old, 31.8% for 71-80 yr old, and 29.4% for patients greater than 80 yr old. Significant decrease ($p = 0.025$) in the overall incidence of hepatic metastases with advancing age was found. This decrease was manifest for all primary tumor locations except for tumors of the stomach and pancreas. There was no statistically significant difference in the incidence of hepatic metastases between men and women. (12 Refs) (In CZE)

34. PROLONGED SURVIVAL OF A PATIENT WITH ADVANCED COLONIC CANCER.

Hsu SD, Schwartze GM, Maxwell VL
Hematology-Oncology Section, Veterans Admin. Medical Center, 300 East Roosevelt Road, Little Rock, AK, 72206
Dis Colon Rectum; 24(8):636-638 1981

A 39-yr-old man who survived 14 yr following the diagnosis of advanced colonic carcinoma is reported. The presence of metastatic lesions had been well documented at the time of abdominal surgery on three different occasions and at autopsy. The possible mechanism for his unusually prolonged survival time is discussed. (Author abstract) (10 Refs)

35. A CASE OF CRONKHITE-CANADA SYNDROME DEVELOPING AFTER HEMI-COLECTOMY.

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Second Dept. Surgery, Sch. Medicine, Fukuoka Univ., 34 Nanakuma, Nishi-ku, Fukuoka 814-01, Japan
Endoscopy; 13(6):251-253 1981

A 57-yr-old male presented with abrupt melena. Numerous polypoid lesions were found in the stomach and colon accompanied by characteristic ectodermal changes of the Cronkhite-Canada syndrome. He had undergone a left side hemicolectomy for colon cancer 3 yr previously. Two mo after the operation, he had noticed hyperpigmentation of the skin, alopecia and chronic diarrhea. Subsequently, after 8 mo, the presence of numerous polypoid lesions in the remnant colon and the rectum was established. This is the first reported case in which features of the Cronkhite-Canada syndrome have developed after resection for colon cancer. (Author abstract) (18 Refs)

36. MELANOTIC ADENOCARCINOMA OF THE ANORECTUM.

Chumas JC, Lorelle CA
Dept. Pathology, Health Sciences Center, State Univ. New York, Stony Brook, NY, 11794
Am J Surg Pathol; 5(7):711-717 1981

The case history of a 56-yr-old man with pigmented adenocarcinoma of the anorectal region is presented. Electron microscope examination of a biopsy specimen showed three distinct cell populations. The majority of cells contained abundant mucin globules intermixed with melanosomes that were surrounded by a double layered membrane. The second population contained isolated melanosomes; these cells were identified as melanocytes. The third very rare cell type contained both mucin and isolated melanosomes. (31 Refs)

37. THE SOFT AGAR CLONOGENICITY AND CHARACTERIZATION OF CELLS OBTAINED FROM HUMAN SOLID TUMORS BY MECHANICAL AND ENZYMATIC MEANS.

Slocum HK, Pavelic ZP, Kanter PM, Nowak NJ, Rustum YM
Dept. Experimental Therapeutics and Grace Cancer Drug Center, Roswell Park Memorial Inst., Bufallo, NY, 14263
Cancer Chemother Pharmacol; 6(3):219-225 1981

A two-step procedure for releasing cells from solid tumors was applied to specimens of human melanoma, sarcoma, lung, colon, and breast carcinoma. The first population released mechanically was compared with the population subsequently released enzymatically in tests of dye exclusion, ribonucleoside triphosphate pool sizes, intactness of DNA, and clonogenicity in soft agar. The number of dye-excluding cells obtained was much greater from the enzymatic than from the mechanical step in the disaggregation procedure. Ribonucleoside triphosphate pools for cells released enzymatically were generally higher, especially in melanoma. Enzymatically and mechanically released populations contained approx the same number of clonogenic cells. Several semisolid media were employed in the tests of clonogenicity. All methods employing an agar underlayer appeared satisfactory and approx equivalent in cloning efficiency. The methyl cellulose-agar systems facilitated manipulation of colonies for implantation into nude mice. Colonies pooled from a single plate produced tumors from human melanoma, sarcoma, and ovarian carcinoma. Median clonogenicities were slightly higher for enzymatically released cells in melanoma, sarcoma, and colon, and lower in lung and breast carcinomas. Less damage to DNA was noticed in cells released enzymatically. Comparison of four different areas of individual tumor specimens were made with cells released enzymatically and measuring cell yield, dye exclusion, ATP pool size, uptake, and metabolism of 5-fluoropyrimidines. Metabolism of fluorinated pyrimidines showed the most variations. (17 Refs)

38. INFLUENCE OF HISTAMINE AND SEROTONIN ANTAGONISTS ON THE GROWTH OF XENOGRAFTED HUMAN COLORECTAL TUMORS.

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Dept. Anatomy, Monash Univ., Clayton, Victoria 3168, Australia
JNCI; 67(6):1207-1212 1981

Four lines of human colorectal cancer were established and serially propagated as subcutaneous xenografts in immunosuppressed inbred CBA/Lac mice. Established xenografts were then used to investigate the influence of a serotonin antagonist (BW 501c) and a histamine H2 receptor antagonist (Cimetidine) on xenograft growth. The growth of each of the four tumor lines was significantly inhibited by BW 501c throughout the treatment, whereas the growth of only two tumor lines was significantly inhibited by Cimetidine treatment. The response of individual tumor lines was not predictable on the basis of either tumor histopathology or the natural growth rate of the untreated xenograft. A number of alternative, but not mutually exclusive, hypothesis are suggested to explain the results. One hypothesis proposes that colorectal tumors are composed of subpopulations of tumor cells that are variously dependent on or independent of amine hormones. Another hypothesis is that tumor cells exhibit temporal changes in hormone sensitivity to amine hormones during treatment. Finally, it is suggested that serotonin and/or histamine H2 antagonists may be useful in preventing the repopulation of colorectal carcinomas following antineoplastic therapy with the use of conventional drugs. (Author abstract) (10 Refs)

39. VARIOUS ISOZYME GENE EXPRESSION PATTERNS AMONG HUMAN COLORECTAL ADENOCARCINOMA CELL LINES AND TISSUES.

Rutzky LP, Siciliano MJ
Dept. Surgery, Univ. Texas Medical Sch. at Houston, Houston, TX, 77030
JNCI; 68(1):81-90 1982

Seven tissue-specific isozymes lactate dehydrogenases A and lactate dehydrogenase B (LDHA and LDHB), esterase B2 and esterase A4 (ESB2 and ESA4), creatine kinase B (CKB), and red blood cell and tissue forms of adenosine deaminase (ADA) were examined in the human adenocarcinoma cell line LS174T and its subclones grown under a wide variety of conditions. Strong expressions of ESB2, ESA4, and CKB were stable in all material studied, as was a greater expression of LDHA than of LDHB. ADA isozyme expression varied with culture conditions. Identical expression of the five stable isozymes was observed in six surgical specimens or normal bowel mucosa, white cell lines derived from normal mucosa varied in the expression of these isozymes. An additional 23 colorectal cell lines, derived from primary or metastatic adenocarcinomas in different stages of invasiveness and differentiation from 18 individuals, were verified as to their origin by genetic signature analysis and similarly studied for isozyme expression. These lines had different, yet stable, gene expression patterns similar to differences observed among six adenocarcinoma surgical specimens. These differences could not be related to the number of passages that the cell lines were in culture nor to the stages of the tumors at the time that the cell lines were initiated or surgical samples tested. Gene expression patterns in adenocarcinomas differed, these differences might have been due to the origin of colorectal adenocarcinomas from different cell types within a heterogeneous mucosa, and the colorectal cell lines studied represented appropriate models for colon cancer. (Author abstract) (53 Refs)

40. HUMAN-TUMOR-DERIVED CELL LINES CONTAIN COMMON AND DIFFERENT TRANSFORMING GENES.

Perucho M, Goldfarb M, Shimizu K, Lama C, Fogh J, Wigler M
Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724
Cell; 27(3):467-476 1981

We have screened different cultured cell lines established from human tumors for the ability of their DNAs to induce transformed foci in NIH/3T3 cells. Based on restriction endonuclease digestions and the presence of human sequences in mouse transformants, we conclude that five of these human tumor cell lines contain a gene or genes capable of transforming mouse cells and that at least three different transforming genes are present in these five lines. Three cell lines, two derived from lung carcinomas and one derived from a colon carcinoma, transfer the same or closely related human genes. If these transforming genes are mediating the tumorigenic state of the human cells, then our results indicate that overlapping pathways leading to tumorigenesis may arise independently. (Author abstract) (32 Refs)

41. TUMOR-ASSOCIATED CHROMATIN ANTIGENS OF HUMAN COLON ADENOCARCINOMA CELL LINES HT-29 AND LOVO.

Duhl DM, Banjar Z, Briggs RC, Page DL, Hnilica LS
Dept. Biochemistry, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
Cancer Res; 42(2):594-600 1982

Antiserum to dehistonized chromatin from human colon adenocarcinoma cell line HT-29 was raised in rabbits and used for the immunodetection of colon tumor-associated nuclear antigens. Quantitative microcomplement-fixation studies indicated that the antiserum had reactivity similar to those of chromatins of two human colon adenocarcinoma cell lines (HT-29 and LoVo) and with nonneoplastic colon. Immunocytochemical localization showed the chromatin antigens to be evenly dispersed throughout the nucleus. Immunochemical staining of electrophoretically separated chromosomal proteins transferred to nitrocellulose sheets revealed several intensely staining antigens predominantly in the mol wt range of 62,000 to 75,000. When the antiserum was immunoabsorbed with nonneoplastic human colon chromatin, two antigens with mol wt of 67,000 and 92,000 were identified only with the tumor chromatins. Antiserum immunoabsorbed with either LoVo or HT-29 chromatin failed to show any immunoreactivity, suggesting that these tumor-associated proteins, or antigenic sites residing on these proteins, are identical in both colon tumor cell lines. (Author abstract) (43 Refs)

42. HETEROGENEITY OF CANCER CELLS FROM A SINGLE HUMAN COLON CARCINOMA.

Dexter DL, Spremulli EN, Fligiel Z, Barbosa JA, Vogel R, VanVoorhees A, Calabresi P

(c/o Calabresi) Dept. Medicine, Roger Williams General Hosp., 825 Chalkstone Ave., Providence, RI, 02908

Am J Med; 71(6):949-956 1981

The human colon carcinoma cell line DLD-1, established from tumor tissue obtained from a 45-yr-old white man with an adenocarcinoma of the sigmoid colon, was studied from the perspective of tumor heterogeneity. The karyotype and morphology of cells from an early passage DLD-1 culture, as well as the histologic features of both the original tumor and neoplasms produced by inoculation of athymic nude mice with DLD-1 cells, indicated that both the DLD-1 cell line and the original tumor were heterogeneous. Two clones were isolated from the DLD-1 line; they differed in their morphology, karyotype, and cloning efficiency in soft agar. Furthermore, when cells from each clone were injected into athymic mice, histologically distinct tumors were produced. Various analyses showed that the two cloned lines were representative of the two subpopulations predominantly responsible for the heterogeneity of the original neoplasm. In vitro drug screening results demonstrated that the two cloned lines have differential sensitivities to chemotherapeutic agents. The parent DLD-1 human colon carcinoma cell line and its two cloned subpopulations provide material for the study of various aspects and implications of human cancer cell heterogeneity. (Author abstract) (28 Refs)

43. VINYLOGOUS CARBINOLAMINE TUMOR INHIBITORS. 8. ACTIVITY OF BIS(ACYLOXYMETHYL) DERIVATIVES OF PYRROLES AND PYRROLIZINES AGAINST A PANEL OF MURINE LEUKEMIAS AND SOLID TUMORS.

Anderson WK, Chang CP, Corey PF, Halat MJ, Jones AN, McPherson HL, New JS, Rick AC

Dept. Medicinal Chemistry, Sch. Pharmacy, State Univ. New York at Buffalo, Cooke-Hochstetter Towers, Buffalo, NY, 14260

Cancer Treat Rep; 66(1):91-97 1982

The activity of three pyrroles and four pyrrolizines is compared in several different experimental leukemias and solid tumors in mice. Two compounds were particularly noteworthy, the bis(N-cyclohexylcarbamate) and the bis[N-(2-propyl)] derivatives of 2,3-dihydro-5-(3,4-dichlorophenyl)-6,7 bis(hydroxymethyl)-1H-pyrrolizine. These two compounds showed a very high level of activity against B16 melanocarcinoma, CD8F1 mammary tumor, colon tumor 26, and colon tumor 38, and a significant number of 'cures' were recorded. The isopropyl compound was more potent than the cyclohexyl compound, but both showed a similar profile of activity. (Author abstract) (15 Refs)

44. IN VIVO KINETICS OF THYMIDYLATE SYNTHETASE INHIBITION IN 5-FLUOROURACIL-SENSITIVE AND -RESISTANT MURINE COLON ADENOCARCINOMAS.

Spears CP, Shahinian AH, Moran RG, Heidelberger C, Corbett TH (c/o Heidelberger), Univ. Southern California Cancer Center, 1721 Griffin Ave., Los Angeles, CA, 90031
Cancer Res; 42(2):450-456 1982

The predictive utility of several biochemical parameters of 5-fluorouracil (5-FUra) action was evaluated in four murine colonic adenocarcinomas: 5-FUra-sensitive tumor 38 and 5-FUra-resistant tumors 07/A, 51, and 06/A. Thymidylate synthetase (TS) was determined by a tritiated 5-fluoro-2'-deoxyuridylate (FdUMP)-binding assay. Bolus 5-FUra (80 mg/kg, ip) administration caused in all tumors a rapid decrease in free TS levels. Only tumor 38, however, showed inhibition of TS to undetectable (less than 0.05 pmol/g) levels, which lasted up to 6 hr after treatment; correction for dissociation of endogenous TS; FdUMP:folate ternary complex during the TS assay was required. Total TS (free enzyme plus ternary complex) was determined with experimental conditions that achieved quantitative recovery of free TS from ternary complex. By 48 hr after 5-FUra, Tumor 38 showed a decrease in total TS proportional to the estimated log kill/dose of 5-FUra; in contrast, the resistant tumors showed no such decrease from pretreatment levels. Assay of FdUMP showed that the free nucleotide was formed rapidly in all tumors in excess over available TS-binding sites. However, tumor sensitivity did not correlate with peak or residual FdUMP levels or with deoxyuridylate levels, which were low and remained so in all tumors. Tumor sensitivity to 5-FUra also could not be explained by the small differences among the tumors in total perchloric acid-soluble metabolites of 5-FUra or drug incorporation into RNA. We conclude from these data that levels of free TS in the tumor after 5-FUra treatment are predictive of chemotherapeutic response in these murine models of human colonic adenocarcinoma. (Author abstract) (50 Refs)

45. IMMUNOTHERAPY OF A MURINE COLON CANCER WITH SYNGENEIC SPLEEN CELLS, IMMUNE RNA AND TUMOR ANTIGEN.

Fukushima M, Colmerauer ME, Nayak SK, Koziol JA, Pilch YH
1st Dept. Surgery, Hirosaki Univ. Sch. Medicine, Hirosaki, Japan
Int J Cancer; 29(1):107-112 1982

In combination with xenogeneic immune RNA (I-RNA) and tumor antigen (TA), syngeneic spleen cells inhibited the growth of a N-methyl-N-nitrosourea-induced colon carcinoma (CT-26) in BALB/c mice. The sequential administration of 1 x 10(7) spleen cells, 1 mg of anti-CT-26 I-RNA and 0.4 mg of CT-26 TA resulted in a 20% survival rate of mice bearing established CT-26 tumors. On the other hand, administration of the spleen cells only, I-RNA only or TA only was not effective in inhibiting tumor growth. Similarly, when any one of the three agents (I-RNA, TA and spleen cells) was omitted, no anti-tumor effect was obtained. A higher dose (1 x 10(8)) and a lower dose (1 x 10(6)) of spleen cells decreased the antitumor effect of this combination therapy. A higher dose (2 mg) and a lower dose (0.5 mg) of I-RNA, as well as a higher dose of TA (0.8 mg) had no influence on the antitumor effect. However, a lower dose of TA (0.2 mg) in combination with spleen cells and I-RNA decreased the antitumor effect. When all three agents were administered at higher or lower doses, no antitumor effect was obtained. When mice bearing CT-26 tumors were treated with spleen cells, plus I-RNA directed against a syngeneic but antigenically different tumor (BP/B/5) and BP/B/5 TA, with spleen cells plus CT-26 I-RNA and BP/B/5 TA, or with spleen cells plus BP/B/5 I-RNA and CT-26 TA, no antitumor effect was observed. These results indicate that the antitumor responses observed were due to tumor-specific immune responses. In conclusion, in order to obtain growth retardation or regression of established CT-26 tumor transplants, the sequential administration of all three agents (spleen cells, I-RNA and TA) was required. The optimal doses of each agent were found to be 1 x 10(7) spleen cells, 0.5 mg or 1 mg of I-RNA and 0.4 mg of tumor antigen. Higher or lower doses decreased the antitumor effect. Tumor-specific immune reactions appeared to be involved. (Author abstract) (21 Refs)

46. EFFECTS OF THREE RETINOIDS ON COLON ADENOCARCINOMAS, SARCOMAS AND HYPERPLASTIC POLYPS INDUCED BY INTRARECTAL N-METHYL-N-NITROSOUREA ADMINISTRATION IN MALE F344 RATS.

Wenk ML, Ward JM, Reznik G, Dean J
Microbiological Assoc., Inc., 5221 River Road, Bethesda, MD, 20816
Carcinogenesis; 2(11):1161-1166 1981

Male F344 rats, 9 wk of age, were given multiple intrarectal administrations of N-methyl-N-nitrosourea (NMU) at 0.5 mg/dose twice a wk for a total of 8, 12, or 16 doses. Five days after the final NMU instillation, rats were placed on one of four diets; chow with retinoid vehicle, chow with 654 mg N-ethylretinamide per kg diet, chow with 686 mg N-(2-hydroxethyl)retinamide per kg diet, or 406 mg retinylidene dimedone per kg diet. Groups of 40-50 rats receiving 16, 12, or 8 total doses were sacrificed 32, 44, or 52 wk after the initial NMU dose, respectively. The number of rats with colon tumors and the number of tumors per tumor bearing rat in each dosage regimen was compared to appropriate controls. Organ weights for testis, liver, and kidneys were similar for controls and retinoid treated animals and no histopathologic lesions indicative of retinoid toxicity were found. Unusual proliferative lesions of the colon in rats of all dosed groups included hyperplastic and inflammatory polyps and sarcomas. The feeding of diets containing these three retinoids did not significantly modify the incidence or multiplicity of colon tumors observed under these conditions. (Author abstract) (18 Refs)

47. EFFECT OF RETINOIDS ON THE INDUCTION OF COLON CANCER IN F344 RATS BY N-METHYL-N-NITROSOUREA OR BY 1,2-DIMETHYLHYDRAZINE.

Silverman J, Katayama S, Zelennkas K, Lauber J, Musser TK, Reddy M, Levenstein MJ, Weisburger JH
American Health Foundation, Naylor Dana Inst. Disease Prevention, Valhalla, NY, 10595
Carcinogenesis; 2(11):1167-1172 1981

The possible modifying effect of synthetic and natural retinoids on the incidence of colon cancer in rats induced by two intrarectal doses of 2.5 mg of N-methyl-N-nitrosourea (MNU) given once a wk for 2 successive wk or a single 150 mg/kg body weight dose of 1,2-dimethylhydrazine (DMH), sc was investigated. Emphasis was on the effect of the development of early tumors as visualized by endoscopy. With the retinoids N-ethyl-retinamide, N-2-hydroxyethylretinamide, N-(4-hydroxyphenyl)-all-trans-retinamide (RAHA) and retinyl acetate (RA) administered orally after the carcinogens, significant differences in early developing tumors were not found. At histopathological examination of the tumors the RAHA + DMH group had significantly fewer adenomas per animal. The percentage of adenoma bearing rats was significantly lower in groups receiving RAHA + DMH or RA + DMH. However, food consumption was lower in rats consuming either RAHA or RA Retinyl palmitate (RP) and RAHA were administered intrarectally to MNU-induced rats either before or after the carcinogen. When administered before MNU, RP caused a significant increase in the percentage of tumor bearing animals and the av number of tumors per animal as visualized endoscopically. At histopathological examination, all retinoid groups except RAHA given after the carcinogen, produced significantly more adenomas per animal and a significantly greater adenoma incidence than did the control groups. Thus, in two systems, the oral administration of retinoids did not clearly inhibit the early or later stages of colon tumor development. Intrarectal infusion of two retinoids had no effect on colonic morphology but at histopathological examination of later stage tumors there was an enhanced adenoma response. (Author abstract) (36 Refs)

48. THE EFFECT OF ADJUVANT IMMUNOTHERAPY ON TUMOR RECURRENCE AFTER SEGMENTAL RESECTION OF CARCINOGEN-INDUCED WISTAR/FURTH PRIMARY BOWEL ADENOCARCINOMAS.

Steele G, Harte PJ, Rayner AA, Corson JM, Madara J, Munroe AE, King VP, Wilson RE

Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115

J Immunol; 128(1):7-10 1982

Primary bowel tumors were induced in Wistar/Furth (W/Fu) rats by 16 weekly sc injections of 1,2-dimethylhydrazine (DMH). After 'curative' resection of primary adenocarcinomas of the colon, 75% of control rats who received no further treatment developed local or regional recurrence within 22 wk. In four separate experiments, rats immunized after primary tumor resection by three weekly sc inoculations of 1 x 10(6) irradiated (10,000 rad) DMH-W15 sarcoma cells (no tumor-associated antigens cross-reacting with bowel adenocarcinomas) developed recurrent tumor at a rate similar to the controls. By contrast, after primary bowel tumor resection, rats immunized with DMH-W163 colon adenocarcinoma (possessing tumor-associated antigens cross-reactive with other W/Fu bowel adenocarcinomas) showed a consistently reduced rate of local or regional recurrence compared to either of the controls (chi2 = 4.62, p less than 0.05) or the rats immunized with sarcomas (chi2 = 5.42, p less than 0.05). By 22 wk after primary tumor resection, only 35% of the DMH-W163-immunized animals in each of the four experiments showed recurrence. No deaths from recurrences were noted in any of the experimental groups after this time, and selected animals sacrificed in the immunized groups up to 30 wk after primary tumor resection were documented to be disease-free. Protection against tumor recurrence was, therefore, a reflection of increased disease-free survival. No change in the effectiveness of immunoprotection in this model could be demonstrated after resection of less invasive primary tumors. These data reflect the utility of a new model in which modification of the natural history of individual primary bowel adenocarcinomas can be examined. The similarities and differences between this system and humans with colon cancer are discussed. (Author abstract) (13 Refs)

49. EFFECTS OF DIETARY BRAN AND THE COLON CARCINOGEN 1,2-DIMETHYLHYDRAZINE ON A FECAL BETA-GLUCURONIDASE ACTIVITY IN MICE.

London JF, Clapp NK, Henke MA

Oak Ridge Graduate Sch. Biomedical Sciences, Univ. Tennessee, Oak Ridge, TN, 37830

Food Cosmet Toxicol; 19(6):707-711 1981

Daily variations in fecal beta-glucuronidase (BGLU) activity in BALB/c mice and variations in BGLU activity induced by different dietary brans and/or 1,2-dimethylhydrazine (DMH) were investigated. The effect of DMH on BGLU was significant. Three mo after DMH treatments, mice had persistently depressed BGLU activity compared to mice not treated with DMH. BGLU activities of animals on control or wheat bran diets were 4-5x higher than the activities in animals on either soya-bean bran or corn-bran diets and differed significantly from them. Animals fed the corn-bran diet consistently had the lowest BGLU activities in fecal stream. No synergistic action of any combination of variables was noted. (63 Refs)

50. ABERRANT AND NONRANDOM METHYLATION OF CHROMOSOMAL DNA-BINDING PROTEINS OF COLONIC EPITHELIAL CELLS BY 1,2-DIMETHYLHYDRAZINE.

Boffa LC, Gruss RJ, Allfrey VG

Rockefeller Univ., New York, NY, 10021

Cancer Res; 42(2):382-388 1982

The alkylating carcinogen 1,2-dimethylhydrazine (DMH) induces colonic tumors with high incidence. The sites of in vivo modification of target macromolecules were studied using [methyl-3H]DMH. Carcinogen binding to subcellular fractions of colonic epithelial cells was analyzed at time intervals ranging from 10 min to 36 hr, with particular emphasis on the alkylation of nuclear constituents. DMH modifies not only nucleic acids but also histones and other DNA-binding proteins in the target cells. Separation of the 3H-methylated amino acids showed aberrant methylation patterns after exposure to [3H]DMH, as compared with methylations observed with [methyl-3H]methionine as a natural methyl group donor. DMH-modified histone H1 contained methylated lysine, arginine, and histidine residues not normally found, and other histones had abnormal methylarginine contents. High-mobility-group proteins and other nuclear proteins contained methyllysine residues not normally detected. Proteins known to be associated with template-active and more accessible DNA sequences, such as the high-mobility group proteins and the multiacetylated forms of histones H3 and H4, were preferentially damaged after exposure to [3H]DMH. The result suggests that carcinogen-induced chromosomal damage is not random and may selectively affect proteins in the actively transcribing or replicating genes in the target cells. That damage affects the amino acids most likely to be involved in DNA binding. (Author abstract) (47 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

51. ADENOCARCINOMA IN PERINEAL FISTULAS OF CROHN'S DISEASE.

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Dis Colon Rectum; 24(8):639-643 1981

Until recently, Crohn's disease has not been regarded as a premalignant lesion, but the increasing number of patients with Crohn's disease in whom adenocarcinoma of the gastrointestinal tract develops strongly suggests that these patients are indeed at a higher risk for carcinoma. These patients are usually young and tend to develop a malignancy in the bypassed ileum or right colon. Patients with such lesions usually have poor prognosis. Adenocarcinoma arising in perineal fistulas secondary to Crohn's disease has not been reported in English medical literature except for one case published in 1975. In this article, the authors report a second, similar case of Crohn's disease with recurrent perineal fistulas. An infiltrating adenocarcinoma developed in these fistulas, in the anorectal region, and in the left labia. The risk of malignancy should be seriously considered in the management of Crohn's disease, especially in young patients. Because of the risk of adenocarcinoma in these patients, resection rather than bypass is recommended in the surgical management. (Author abstract) (14 Refs)

52. A COMPARISON OF CANCER RISK IN CROHN'S DISEASE AND ULCERATIVE COLITIS.

Greenstein AJ, Sachar DB, Smith H, Janowitz HD, Aufses AH
Dept. Surgery, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY, 10029
Cancer; 48(12):2742-2745 1981

The authors estimated cancer risk among 579 patients hospitalized with Crohn's disease between 1960-1976 by calculating the ratios of observed number of cancers (O) in our hospital sample to the expected number of cancers (E) based on the age- and sex-specific cancer rates of a standard population. The authors then compared these O/E ratios with the O/E ratios similarly calculated among 267 patients hospitalized with ulcerative colitis. The risk of colorectal cancer was significantly increased in Crohn's disease (O/E = 6.9, p less than 0.001). This increase was similar in magnitude to that found in left-sided ulcerative colitis (O/E = 8.6, p less than 0.001) but was much less than that found in universal ulcerative colitis (O/E = 26.5, p less than 0.001). The incidence of small bowel cancer was greatly increased in the combined group of regional enteritis and ileocolitis (O/E = 85.8, p less than 0.001), and even more so in the regional enteritis group alone (O/E = 114.5, p less than 0.001). The incidence of extraintestinal cancer did not increase in any of the patient groups. (Author abstract) (23 Refs)

53. THE LOW INCIDENCE OF COLORECTAL CANCER IN A 'HIGH-RISK' POPULATION: ITS CORRELATION WITH DIETARY HABITS.

Rozen P, Hellerstein SM, Horwitz C
Ichilov Hosp., Weizmann St., Tel Aviv, Israel
Cancer; 48(12):2692-2695 1981

In Israel, the incidence of colorectal cancer is highest in European-American-born Jews, although this incidence is lower than that found in European-born Jews living in the United States. A significantly lower-than-expected incidence was found in a specific kibbutz established by immigrants of European origin. Matched population samples from this kibbutz and the city of Tel Aviv revealed significant differences in dietary habits. The kibbutz members ate more unavailable carbohydrate and ascorbic acid and had a higher dietary polyunsaturated to saturated fat (P/S) ratio than the city dwellers. Both groups ate more crude fiber, less saturated fat, and less beef than has been reported from America and European countries. This kibbutz diet seems to have prevented large bowel cancer, parallels the 'prudent' diet of Wynder, and possibly indicates the feasibility of colorectal cancer prevention. (Author abstract) (34 Refs)

54. DIETARY FIBER: IS IT REALLY HELPFUL?

Burkitt DP
Unit Geographical Pathology, St. Thomas's Hosp., London SE1, England
Geriatrics; 37(1):119-122,126 1982

Fiber in the diet is discussed; topics include defects of Western diet, cancer, diabetes, gallstones, obesity, ischemic heart disease, and history of disease. Culturally determined dietary patterns appear to be responsible for the high prevalence in Western societies of major diseases such as colon cancer, atherosclerotic heart disease, and diabetes. Five fundamental dietary changes that distinguish modern Western diets from those of the Third World. are reduction in consumption of carbohydrate, particularly starch, increased consumption of sugar, increased consumption of fat, increased consumption of salt, and reduced consumption of fiber and replacement of fiber derived from cereals, legumes, and tubers with that from fruits and leafy vegetables. Cereal fiber has a much greater influence on bowel content and behavior than that from fruits and leafy vegetables. Fiber has important mechanical and metabolic functions in addition to influencing the bacterial flora in the large bowel. Fiber-rich diets are believed to protect against large-bowel cancer and may provide some general protection against all diet-related cancers. The role of dietary fiber in other diseases is reviewed. Diets should include more starch, less sugar, less fat, more fiber, and less salt. (10 Refs)

55. EPIDEMIOLOGIC STUDY OF DRINKING WATER CHLORINATION AND WISCONSIN FEMALE CANCER MORTALITY.

Young TB, Kanarek MS, Tsiatis AA
Dept. Preventive Medicine, Univ. Wisconsin, 504 North Walnut St., Madison, WI, 5 3706
JNCI; 67(6):1191-1198 1981

The association between gastrointestinal, urinary tract, brain, lung, and breast cancer mortality and drinking water trihalomethane exposure, as estimated by av daily chlorine dosage of water source 20 yr past, was investigated for Wisconsin white females by use of a death certificate-based case-control study design. A total of 8,029 cancer deaths and 8,029 controls (noncancer deaths) matched on county of residence, year of death, and age were taken from mortality records of 28 counties for the years 1972-77. Data on characteristics and treatment of municipal water supplied to the residences of cases and controls were obtained from questionnaires sent to the water superintendents of the 202 waterworks associated with the sample. By the use of logistic regression analysis, odds ratios for site-specific cancer death associated with high, medium, and low chlorine-dosed water as compared to unchlorinated water exposure were determined; the control variables were urbanicity, marital status, and occupation. With the exception of cancer of the colon, no anatomic cancer site was significantly associated with any chlorine dose exposure category. For colon cancer, odds ratios of 1.51 [95% confidence interval (CI) = 1.06-2.14], 1.53 (95% CI = 1.08-2.0) and 1.53 (95% CI = 1.11-2.11) were obtained for high-, medium-, and low-dose chlorination, respectively (p less than or equal to 0.02). For colon cancer cases and controls exposed to water sources affected by rural runoff, odds ratios of 3.30 (95% CI = 1.45-7.48), 3.60 (95% CI = 1.57-8.26), and 2.74 (95% CI = 1.10-6.88) were observed for high, medium, and low chlorine dosages 20 yr past (p less than 0.025). (Author abstract) (40 Refs)

56. SERUM CHOLESTEROL AND COLON CANCER INCIDENCE IN HAWAIIAN JAPANESE MEN.

Stemmermann GN, Nomura AM, Heilbrun LK, Pollack ES, Kagan A
Kuakini Medical Center, 347 North Kuakini St., Honolulu, HI, 96817
JNCI; 67(6):1179-1182 1981

A prospective study of cancer and coronary heart disease (CHD) in 8,006 Hawaiian Japanese men, aged 45-68 yr, showed that serum cholesterol levels below 180 mg/dl predicted low rates of CHD and high rates of colon cancer. Men with colon cancer had lower mean serum cholesterol levels than did other members of the cohort, including those with cancer at other sites. The lowest serum cholesterol levels were obtained from men who died as a result of colon cancer. The lack of such an association with other cancers and the persistence of this inverse association in colon cancer patients diagnosed 5-9.9 yr after examination suggest that the low serum cholesterol was not due to preexisting disease. Right colon tumors showed the strongest inverse association with serum cholesterol. The differences between CHD and colon cancer in respect to serum cholesterol indicate that different subsets of the westernized Japanese populati on are affected. (Author abstract) (12 Refs)

57. TRENDS IN THE ANATOMICAL DISTRIBUTION OF COLORECTAL CARCINOMA IN HAWAII, 1960-1978.

Nomura AM, Kolonel LN, Hinds MW

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Dig Dis Sci; 26(12):1116-1120 1981

The incidence of colorectal adenocarcinoma increased in the five major ethnic groups in Hawaii, but more in men than women. The highest rates were in the Chinese and Japanese. The site-specific time trend patterns revealed that the greatest increase occurred in rectosigmoid cancer, followed by cancer of the sigmoid colon and the transverse descending colon. Rectal cancer had minimal changes in rats over time. The comparison of site-specific rates between the Japanese in Hawaii and Miyagi Prefecture, Japan, showed that the occurrence of cancer of the rectosigmoid, sigmoid, and transverse descending colon was far greater in Hawaii than Miyagi with minimal differences in the rates of rectal cancer. The findings from this study indicate that the separate anatomical locations of colorectal cancer probably have some distinct etiologies that need further investigation. (Author abstract) (5 Refs)

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Diagnosis, Treatment

SERIES CT07 No. 82/06

JUNE, 1982

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. DISTRIBUTION OF POLYPS IN THE LARGE BOWEL IN RELATION TO AGE: A COLONOSCOPIC STUDY.

Granqvist S
Dept. Diagnostic Radiology, Huddinge Univ. Hosp., Huddinge, Sweden
Scand J Gastroenterol; 16(8):1025-1031 1981

In a colonoscopic study of the anatomical distribution of 600 adenomas, polyps of all sizes in patients up to 55 yr old were predominantly located distally. With advancing age of the patients a successively greater proportion of at first small and then also larger polyps was found in the intermediate and proximal parts of the colon. These findings support the assumption that polyps of the gut as a rule originate in the distal part of the large bowel, only later to appear proximally. This concept is important, since it might serve to explain conflicting experience with regard to the site of colorectal tumors. (Author abstract) (25 Refs)

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2. IN VIVO RADIOIMMUNODETECTION OF OCCULT RECURRENT COLONIC CARCINOMA.

DeLand FH, Kim EE, Primus FJ, Dine ME, Goldenberg DM
Veterans Admin., Lexington, KY, 40536
AJR; 138(1):145-148 1982

External imaging of radionuclide-labeled antibodies to carcinoembryonic antigen (CEA) was used to detect and localize metastatic carcinoma in a 57-yr-old woman with a rising and markedly elevated plasma CEA level 5 mo after anterior resection of an adenocarcinoma of the sigmoid colon. Other extensive radionuclide evaluations were not helpful in determining the cause plasma CEA elevation. The value of in vivo radioimmunodetection for the demonstration of CEA-containing neoplasms is discussed. (16 Refs)

3. CLASSIFICATION OF COLORECTAL CARCINOMAS WITH REGIONAL LYMPHATIC METASTASES.

Hermanek P, Altendorf A
Abteilung fur Klinische Pathologie, Chirurgischen Klinik der Universitat Erlangen-Nurnberg, Maximiliansplatz, 8520 Erlangen, W. Germany
Pathol Res Pract; 173(1/2):1-11 1981

According to the UICC classification of colorectal carcinoma patients with histologically confirmed regional lymph node metastases (pN1) are not further subdivided. In these patients, however, subgroups with widely differing prognosis can be established. A number of classifications proposed to cover these patients are discussed. The analysis of the Erlangen case material shows that it is decisive for the prognosis to know whether involved lymph nodes are located only at the branches of the supplying vessels ('peripheral') or whether the lymph nodes along the trunks of these vessels ('proximal') are also involved. Among the patients with proximal lymph node metastases, the question as to whether the lymph node at the margin of the resected lymph drainage area ('marginal node') is involved or not, has no essential influence on the prognosis. The counting of metastatic lymph nodes does not represent an essential criterion for prognosis. (Author abstract) (19 Refs)

4. THE OCCURRENCE OF SEVERE EPITHELIAL DYSPLASIA AND ITS BEARING ON TREATMENT OF LONGSTANDING ULCERATIVE COLITIS.

Kewenter J, Hulten L, Ahren C
Dept. Surgery III, Sahlgrenska sjukhuset, S-413 45 Goteborg, Sweden
Ann Surg; 195(2):209-213 1982

One hundred twenty-four patients with extensive ulcerative proctocolitis were operated upon with proctocolectomy. The mean observation time was 10.3 yr. Before surgery rectal biopsies were taken in all patients. The relationship between precancerous lesion in rectal biopsies and the presence of precancer and/or cancer in the rectum or colon in the removed specimen was evaluated. Thirteen out of 14 patients showed evidence of severe rectal dysplasia as well as severe dysplasia in the large bowel specimen, and 5 of these patients had a carcinoma as well. The 14th patient showed severe dysplasia only in the rectum as well as a rectal carcinoma. Of 110 patients without severe rectal dysplasia, 36 showed evidence of severe colon dysplasia, and 3 of these patients had a large bowel carcinoma as well. Only one patient had a large bowel carcinoma without evidence of severe dysplasia in the rectum or colon. Thus, 9 patients out of 10 with large bowel carcinoma showed severe dysplasia in rectum and/or colon. Four of these carcinomas were unknown before surgery. Although severe dysplasia in the rectal biopsy is a strong indication of a large bowel carcinoma (6/14), a negative rectal biopsy does not exclude a large bowel carcinoma (4/110). Proctocolectomy cannot be looked upon only as a prophylactic procedure in patients with severe dysplasia in the rectal biopsy, but also as an attempt to curative surgery, as large bowel carcinoma may have already developed in a considerable number of patients where precancer is diagnosed in biopsies. (Author abstract) (24 Refs)

5. FIBROCOLONOSCOPIC AND HISTOLOGICAL CHARACTERISTICS OF TRUE POLYPS OF THE LARGE INTESTINE.

Bakalov V, Velev G, Ianchev V
Inst. Gastroenterology, Sofia, Bulgaria
Vutr Boles; 20(3):23-29 1981

Seventy-six patients (51 men, 25 women; 21-83 yr old) with true polyps of the large intestine are reviewed. At fibroendoscopy, a total of 108 polyps were detected in the cecum (2.8%), ascending colon (11.1%), transverse colon (13.9%), descending colon (19.4%), sigmoid colon (40.8%), and rectum (12%). The sizes of the polyps ranged from less than 0.5 cm (47), to 0.5-1 cm (44), and greater than 1 cm (17); there were 79 pedunculated polyps and 29 polyps on a wide base. Histological examination of biopsy specimens showed that 73.3% of the polyps were adenomatous, 17.2% were adenovillous, and 9.5% were villous. The patients with large (greater than 1 cm) polyps were subjected to endoscopic polypectomy. (21 Refs) (In BUL)

6. COLONIC VILLOUS ADENOMA. MONOCLONAL ORIGIN.

Adolphson CC, Prchal JT, Carroll AJ
(c/o Prchal) Div. Hematology-Oncology, Univ. Alabama in Birmingham, Birmingham, AL, 35294
JAMA; 247(6):829-830 1982

A colonic villous adenoma removed from a glucose-6-phosphate dehydrogenase (G6PD) heterozygous patient was studied. The mucosal cells were separated to eliminate the contaminating nonadenoma cells by enzymatic disaggregation followed by isokinetic gradient centrifugation. The mucosal cells from this colonic polyp contained a single G6PD isoenzyme. Our study demonstrates clonality of this type of polyp and the value of the cell separation techniques in the experimental oncology. (Author abstract) (8 Refs)

7. MALIGNANT CARCINOID TUMORS IN CHILDREN.

Chow CW, Sane S, Campbell PE, Carter RF
Dept. Anatomical Pathology, Royal Children's Hosp., Parkville, Victoria 3052, Australia
Cancer; 49(4):802-811 1982

The clinical, light microscopic, and ultrastructural features of four malignant carcinoid tumors in children, three boys and one girl ages 8-14 years, are described. Extensive metastases to multiple organs were present in three, and in the fourth child there was diffuse local infiltration of the bowel wall, which resembled a lymphoma. The primary tumor arose in the ileum in one child and in the transverse colon in another. In two children, the primary sites could not be determined; one patient is still alive and in the other, permission for autopsy was refused. Electron microscopy showed moderate numbers of neurosecretory granules in some cells in all cases. One patient with extensive metastases showed repeated partial response to radiotherapy and chemotherapy. Eight benign appendiceal carcinoids were seen at the same hospital over the same period, suggesting malignant carcinoids may be more common in children than often assumed. (Author abstract) (20 Refs)

8. HISTOCHEMICAL PROPERTIES OF MUCUS IN EPITHELIAL TUMORS OF THE LARGE INTESTINE.

Jirkova A

Katedra patologie ILF, U nemocnice 4, 128 52 Praha 2, Czechoslovakia

Cesk Patol; 17(3):117-122 1981

Histochemical characteristics of mucus from 23 polyploid adenomas of the rectum and 27 adenocarcinomas (AC) of the colon were studied. Specimens were stained with PAS and alcian blue-pH 2.5 (PAS-AB) for differentiation of neutral and acidic mucus; alcian yellow-pH 2.5 and alcian blue-pH 1 (AY-AB) for differentiation of slightly acidic sialomucins to strongly acidic sulfomucins; high-iron diamine alcian blue-pH 2.5 (HID-AB) for differentiation of sialomucins and sulfomucins; and periodate borohydride KOH PAS (PB KOH PAS) for detection of O-acetyl esters of sialic acid. Malignant transformation of the colon was marked by the disappearance of O-acyl esters of sialic acid. O-acyl esters were detected focally and primarily extracellularly using periodate borohydride KOH PAS staining in 37% of cases. Tubular AC (16 cases) were marked by mixed mucus with varying content of PAS-positive mucosubstances: PAS AM staining produced bluish violet to magenta coloration. Sulfomucins were not detected in tubular AC. O-acyl esters of sialomucin were detected in two AC. Papillary carcinomas (PC: seven cases) produced mucus with more acidic properties than tubular AC. The majority of PC showed intense mucus production, as did villous adenomas. Results indicate a histogenetic relationship between PC and villous adenomas. (15 Refs) (In CZE)

9. VERSATILITY OF BIOTIN-LABELED LECTINS AND AVIDIN-BIOTIN-PEROXIDASE COMPLEX FOR LOCALIZATION OF CARBOHYDRATE IN TISSUE SECTIONS.

Hsu SM, Raine L

Dept. Pathology, Rhode Island Hosp., and Brown Univ., Providence, RI

J Histochem Cytochem; 30(2):157-161 1982

Carbohydrate residues in tissue can be localized by a very sensitive, specific, and simple technique, utilizing a biotin-labeled lectin followed by an avidin-biotin-peroxidase complex (ABC). Distribution of peanut receptors in benign and malignant tissues was found to be quite different. Normal colonic mucosa occasionally shows small dot staining in the supranuclear cytoplasm, while the tumor cells of colonic adenocarcinoma tend to show diffuse cytoplasmic or membranous staining. Normal breast ductal epithelium shows membranous staining at luminal borders, while medullary carcinoma of the breast shows distinct membranous and cytoplasmic staining. The use of this avidin-biotin-peroxidase complex technique may contribute to understanding the process of tumorigenesis as well as providing a sensitive method to determine early stages of malignant transformation. (Author abstract) (9 Refs)

10. ASSOCIATION OF CEA TEST AND LIVER SCAN IN DETECTION OF HEPATIC METASTASES OF GASTROINTESTINAL CARCINOMA.

Buraggi GL, Bombardieri E, Castellani MR, Rodari A, Crippa F

Divisione di Medicina Nucleare, Instituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy

Tumori; 67(6):553-558 1981

The authors evaluate the combined use of liver scan and the CEA test in the diagnosis of hepatic metastases of carcinoma of the gastrointestinal tract. Association of the two tests is justified by the fact that the liver scan is very specific but not very sensitive, whereas the CEA test is more sensitive and not very specific. The sensitivity of the CEA test, on the other hand, can be increased by increasing the threshold of normality. However, the associated diagnostic use of the liver scan and the CEA test gives a loss of specificity with respect to the use of the liver scan alone. The present study, carried out on a series of 376 patients affected by gastrointestinal tumors of which 79 were of the stomach (9 with hepatic metastases), 133 of the colon and higher sigmoid (25 with hepatic metastases), and 164 of the lower sigmoid and rectum (29 with hepatic metastases), proposed to establish by use of a statistical method the optimal threshold of the CEA test that would give the best diagnostic specificity of the combined CEA test and liver scan without any relevant loss of sensitivity. A threshold of 26 ng/ml of the CEA test gave a specificity of 92%, a sensitivity of 80%, and an accuracy of 90%. The authors think that in the detection of live metastases of gastrointestinal tumors, the combined test can be more helpful the less the probability, for a given patient, for other metastatic localizations. (Author abstract) (26 Refs)

11. A PROSPECTIVE ANALYSIS OF LABORATORY TESTS AND IMAGING STUDIES TO DETECT HEPATIC LESIONS.

Kemeny MM, Sugarbaker PH, Smith TJ, Edwards BK, Shawker T, Vermess M, Jones AE

(c/o Sugarbaker), NIH, Building 10, Room 10N116, Bethesda, MD, 20205

Ann Surg; 195(2):163-167 1982

A prospective study of ability of laboratory tests and liver imaging tests to detect hepatic metastases was performed. Eighty patients at risk for hepatic metastases but without clinical evidence of disease were tested with 13 laboratory tests and 3 liver imaging tests. No single laboratory test had greater than 65% accuracy in the detection of hepatic lesions. No combination of the laboratory tests increased this accuracy. If the laboratory tests were used with one of the liver imaging tests, the accuracy was improved in some combinations to 76%. The CEA assay when analyzed in patients with colorectal primaries had an accuracy of 79%. The results show that the laboratory tests alone are not sufficiently accurate to detect liver metastases. Additional accuracy can be obtained by the combined use of a single liver imaging test and selected laboratory tests. Use of all the liver imaging tests and laboratory tests lowers the accuracy and increases the expense and thus is unnecessary. (Author abstract) (22 Refs)

12. ENZYMATIC LABELING OF CARCINOEMBRYONIC ANTIGEN WITH IODINE-125.

Siuda A, Lucka B, Russin K
Radioisotope Production and Distribution Center, Inst. Nuclear Res., Swierk 05-400 Otwock, Poland
J Labelled Comp Radiopharm; 18(12):1797-1807 1981

Lactoperoxidase was used to label carcinoembryonic antigen (CEA) from human hepatic metastases of colonic carcinoma with 125-I. Labeled CEA was purified by gel permeation chromatography and isolated by Sephacryl-S-200 column chromatography. Approx three I atoms were incorporated per CEA molecule; 125-I CEA retained 0.6 of its original immunological activity after 2 mo, and was stable at room temperature. (17 Refs)

13. DETERMINATION OF ESTROGEN RECEPTOR IN HUMAN COLON CANCER TISSUE WITH LABELED FLUORESCENCE ESTRADIOL (FLUORESCEIN ISOTHIOCYANATE).

Zhu N, Cai X, Wu L
Dept. Cancer Res., Second Hosp., Zhejiang Medical Univ., Hangzhou, People's Republic of China
Chin Med J [Engl]; 94(9):607-610 1981

Labeled fluorescence estradiol was used for determination of estrogen receptors (ER) in 33 specimens of colonic cancer. Ten specimens were ER positive. Of 10 specimens, 8 had histology of adenocarcinoma and 2 had histology of mucoadenocarcinoma. (10 Refs)

14. IMMUNE COMPLEXES AND HUMAN NEOPLASIA. DETECTION AND QUANTITATION OF CIRCULATING IMMUNE COMPLEXES BY THE FETAL LIVER CELL ASSAY.

Salinas FA, Wee KH, Silver HK
Cancer Control Agency British Columbia, 2656 Heather St., Vancouver V52 3J3, Canada
Cancer Immunol Immunother; 12(1):11-19 1981

Mouse fetal liver cells (FLC) were used in development of a radioimmunoassay (RIA) for circulating immune complexes (CIC). The uptake of 125I-antihuman IgG by FLC preincubated with sera from patients with various disorders was used to quantitate CIC. Results from unfractionated aggregated human gamma globulin (AHG) and aggregates of defined size were higher with the FLC-RIA than with the Raji assay. FLC-RIA revealed elevated CIC in cancer patients as follows: malignant melanoma, 64/76, breast carcinoma, 38/77, ovarian carcinoma, 40/86, lung carcinoma, 5/17, colon carcinoma, 9/12, and testicular carcinoma, 3/4. The FLC/RIA and Raji tests were compared using 76 serum samples; results were generally in agreement, but FLC-RIA was more sensitive in quantitation of CIC for fewer and smaller immune complexes, conditions in which the Raji assay is reportedly relatively insensitive. (50 Refs)

15. IMMUNE RESPONSES IN CARCINOMA OF THE COLON AND RECTUM.

Greco RS
Dept. Surgery, Div. General Surgery, Rutgers Medical Sch., CMDNJ, P.O. Box 101, Piscataway, NJ, 08854
J Med Soc NJ; 79(1):19-22 1982

Cell-mediated immunity (CMI) after surgery in patients with carcinoma of the colon (CC) or rectum (CR) was compared with CMI in normal patients. CMI was measured by leukocyte migration inhibition assays (Lmi) using KCl extracts of tumor tissue. Of forty patients without malignant lesions, infections, or therapy-induced immunosuppression who underwent elective surgery, 27 showed positive Lmi prior to surgery. Of these, 23 showed negative Lmi immediately after surgery; 4 were positive. Lmi turned positive in 10 patients by 30 days after surgery and in 9 patients within 60 days after surgery; Lmi remained negative after 60 days in 4 patients. Patients with CC showed significant positive Lmi against autologous tumor extracts prior to surgery and immediately afterwards. Lmi turned negative during the late postoperative period. Patients with CR showed no significant positive Lmi against autologous tumor extracts at any time. Neither CC nor CR patients showed positive Lmi against allogeneic tumor extracts at any time, suggesting that each tumor was immunologically distinct. Comparison of Lmi in 20 patients undergoing electrocoagulation of CR with Lmi in 20 patients undergoing abdominoperineal or lower anterior resection showed that electrocoagulation had no effect on cellular immunity. Results indicate that surgery and anesthesia have an immunosuppressive effect and that differences in survival between patients with CC and those with CR may be due to differences in immunocompetence. (8 Refs)

16. DISCREPANCY IN RESULTS FROM THREE GUAIACUM RESIN TESTS.

Feneyrou B, Bories P, Pomier-Layrargues G, Michel H, Gravagne G
Clinique des Maladies de l'Appareil Digestif, Hopital Saint-Eloi, 34059 Montpellier, France
Br Med J; 284(6311):235-236 1982

Results obtained with three guaiacum resin tests, used to detect occult blood loss due to asymptomatic cancer and precancerous lesions of the colon and rectum, are reported. Seventy-five patients, including 33 with colonic lesion (7 with cancer) were tested. HemoFEC and Haemoccult both detected 3/7 cancers and 1/11 cases of polyps. Fecatest detected 5/7 cancers and 4/11 cases of polyps. False negative results occurred in 36% of the tests. Fecatest produced a large number of false positive results. Screening a large number of patients with these tests would entail a commitment to more complicated testing, thereby compromising the implied simplicity of a massive screening protocol. (4 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

17. RESULTS OF TREATMENT OF RECTAL CANCER IN ELDERLY PATIENTS.

Knysh VI, Ozhiganov EL
Dept. Proctology, All-Union Cancer Res. Center, Moscow, USSR
Khirurgiia (Mosk); (11):31-36 1981

Of 736 patients with rectal cancer treated between 1953 and 1978, 276 were greater than 60 yr. Majority of the patients (93.3%) had adenocarcinomas; 47.5% were in Stage III and 28.6% were in Stage IV. Concomitant atherosclerosis was diagnosed in 86.2% of the patients. Surgery was performed in 221/276 patients: 83 underwent abdominal-perineal extirpations (14.5% died), 21 underwent anterior resections (19.0% died), 27 underwent Hartmann's resection (22.2% died), 13 underwent abdominal-anal resections (7.7% died), 8 underwent limited operations (all survived surgery), and 69 underwent palliative surgery (11.6% died). The overall resectability in elderly patients (55.1%) was lower than that in the patients less than 60 yr (65.6%). The 5-yr survival rate in elderly patients was comparable to that in the patients less than 60 yr (64.7% and 55.4%, respectively); the 10-yr survival rates were 48.0% and 44.6%, respectively. Recurrences after radical surgery were observed in 11.4% of elderly patients, compared with 22.9% in the patients less than 60 yr. (19 Refs) (In RUS)

18. RESECTION OR EXTIRPATION OF THE RECTUM IN RECTAL CARCINOMA?.

Herfarth C, Betzler M
Chir. Univ.-Klinik, Im Neuenheimer Feld, D-6900 Heidelberg, W. Germany
Fortschr Med; 99(47/48):1973-1976 1981

Rectal carcinoma (RC) was treated in 87 patients by abdominoperineal rectal extirpation (ARE) and in 75 patients by anterior rectal resection (ARR). Results of ARE and ARR were equivalent. More recurrences and distant metastases occurred after ARE due to a higher proportion of advanced cases. Recurrence and metastasis after either procedure was related to tumor location, stage, and grade. ARR is recommended for RC of the mid- or upper-rectum. (7 Refs) (In GER)

19. PROPHYLAXIS OF LYMPHOGENIC METASTASIS DURING SURGICAL TREATMENT OF RECTAL CANCER.

Brusilovskii MI, Eropkin PV, Odariuk TS, Shliatsis OK, Kapuller LL
Surgical Dept., Res. Inst. Proctology, Moscow, USSR
Khirurgiia (Mosk); (11):36-40 1981

Efficacy of preoperative endolymphatic administration of blocking agent dibunol was evaluated in 52 patients (28 men, 24 women; 30 were greater than 50 yr) with rectal cancer. Histologically, 35 patients had adenocarcinomas, 14 had mucinous carcinomas, and 3 had squamous cell carcinomas; 20 had metastases in the regional lymph nodes. Dibunol dissolved in the iodinated oil showed homogenous accumulation in all groups of lymph nodes, including the para-aortal lymph nodes. The patients were subjected to surgery on day 7-21 after dibunol administration: 36 underwent abdominal-perineal extirpation, 20 underwent extended surgery with aorto-iliac-pelvic lymphadenectomy, 13 underwent abdominal-anal resection, and 3 underwent anterior resection. Histological examination of removed lymph nodes showed marked sclerotic changes, ectasia of the sinuses, atrophy of the lymphoid tissue, and obliteration of the lymphatic vessels. The 1-and 2-yr survival rates were followed-up in 33 patients: only 2/33 developed local recurrences and distant metastases, compared with 9/33 in control patients subjected to radical surgery alone. (20 Refs) (In RUS)

20. DIASTATIC PERFORATION OF THE COLON DUE TO NEOPLASM.

Tissot E, Champetier JP, Vignal J
Service de Chirurgie, Hopital Ed.-Herriot, 69374 Lyon Cedex 2, France
Lyon Chir; 77(6):351-352 1981

Five hundred and thirty-eight patients underwent surgery for confirmed or tentatively diagnosed colorectal carcinoma. Diastatic colonic perforation was found in 9/538 patients (6 men and 3 women, 21-80 yr old, av age 58 yr). Colonic symptoms were observed in six patients, septic shock in three. The cancer was located in the sigmoid colon in seven cases, in the descending colon and in the left colic flexure in one each. The perforation was distant of the tumor in six patients and close to the tumor in three patient, all three having cancer of the sigmoid colon. The perforation was solitary and located in the cecum in four patients. The colonic tumor was revealed by the perforation in two patients. Exclusive cecostomy proved to be ineffective. Cecostomy associated with transverse colostomy was found not to be an adequate technique for the treatment of ischemic lesions of the intestinal wall caused by distension. Subtotal colectomy in operable patients is suitable for the treatment of both the perforation and underlying disease. The findings indicate that in order to prevent such a serious complication, it is better not to delay the surgical treatment of an occlusive colonic cancer. (3 Refs) (In FRE)

21. SURGICAL TREATMENT OF PERFORATION OF THE COLON AND POSTOPERATIVE OUTCOME.

Bustamante I, Kummer D, Pick C
Chir. Univ.-Klinik, Calwer Strass 7, D-7400 Tubingen, W. Germany
Med Welt; 32(48):1837-1838 1981

An attempt was made to identify the method of choice for treatment of perforation of the colon. A retrospective analysis of the outcome of treatment in 206 patients was performed . The most frequent causes of the perforations were diverticulosis (61 patients), carcinoma (54), trauma (26), and iatrogenic perforation (23). The interval between the perforation and surgical treatment was less than 6 hr in cases of iatrogenic perforation or trauma, but was usually more than 12 hr in other causes of perforation. Among the cancer patients, the most common sites of the perforations were the sigmoid or rectosigmoid colon (35) and the cecum (6). Twenty-one of the cancer patients had local peritonitis, and 18/21 underwent simple surgical procedures with formation of an artificial anus. Twenty-two of the cancer patients with diffuse peritonitis also underwent this form of treatment. The lethality was 44% for all cancer patients with local peritonitis and 0% for those with local peritonitis who underwent radical surgical treatment. For the cancer patients with diffuse peritonitis, the lethality was 72% overall and 10% for those who underwent radical surgery. The lethality was 33.5% for all of the patients with perforations of the colon. The grade of peritonitis was the factor that had the greatest effect on prognosis. For all of the noncancer patients, the choice of surgical procedure did not influence the rates of survival. (27 Refs) (In GER)

22. PRESURGICAL PREPARATION OF THE COLON. A CONTROLLED, PROSPECTIVE, MULTICENTER STUDY OF 215 PATIENTS.

Champault G, Adloff M, Alexandre JH, Arnaud JP, Boutelier P, Chevrel JP, Lagache F, Paillier JL, Patel JC, Rignault D, Stoppa R, Triboulet J, Verhaeghe P
Service de chirurgie, Hopital Jean-Verdier, F 93140 Bondy, France
J Chir (Paris); 118(11):677-684 1981

Three different protocols for colon surgical preparation were compared. Group I received standard antibiotic preparation (neomycin and metronidazole) prior to surgery. Group II received a 10% mannitol soln for preparative irrigation. Group III was given antibiotics and mannitol irrigation. Patients with colorectal cancer (158) comprised the greatest number (73.4%) of all surgical cases and included 58/77 patients in Group I, 55/72 in Group II, and 45/66 in Group III. Colon emptying was judged excellent in 50% (Group II) and 57% (Group III) of the patients prepared with mannitol irrigation compared with 16.8% in Group I. There was no difference observed in the intestinal flora of the three groups. No significant differences were noted in the frequency or severity of postoperative infections after conventional preparation by digestive tract irrigation with or without intestinal antibiotics. Regardless of the lesion and its site, the use of antibiotics reduced the incidence of postoperative sepsis. Good results were obtained in 96.1% of Group I, 90.2% of Group II, and 98.4% of Group III. It is suggested that mannitol irrigation provides a modest advantage for patients prepared for colon surgery. (9 Refs) (In FRE)

23. PRIMARY PERINEAL CLOSURE FOLLOWING ABDOMINAL PERINEAL EXCISION OF THE RECTUM FOR CANCER.

Campion JP, Julou P, Launois B
Clinique Chirurgicale, Centre Hospitalier Regional, Hopital Pontchaillou, Rue Henri Le Guillou, 35033 Rennes, France
Ann Chir; 35(10):864-867 1981

The surgical results of 93 primary perineal closures following abdominoperineal excision of the rectum for carcinoma are analyzed. Av patient age was 64.86 with extremes of 40 and 83 yr, and the ratio of men to women was 2:1. Patients were grouped according to quality of healing. Group I included 43 patients (46.25%) with excellent healing. Group II included 22 patients (23.65%) with satisfactory healing in which partial disunion occurred. Group III included 28 patients (30.10%) with unsatisfactory healing in which total disunion and serious complications occurred. There were no significant differences in age or sex among the groups. Groups II and III contained more patients with diabetes and a history of presurgical irradiation. There were three deaths in Group III due to progessive cachexia compared with one death in Group I from a cerebral vascular accident and no deaths in Group II. Two cases of perineal strangulation of the small intestine through the pelvic peritoneum occurred in Group III. Urinary retention affected 23 patients divided equally among the three groups. Better surgical results were associated with a single team approach than with a double team approach. Shorter hospitalization and postoperative treatment time were associated with successful results. (4 Refs) (In FRE)

24. EXPERIENCE WITH A NEW DEVICE FOR COLOSTOMIZED PATIENTS: EXTERNAL MAGNETIC RING.

Desaive CJ, Louis JC
Inst. Surgery, Univ. Liege, Bd. de la Constitution 66, B-4020 Liege, Belgium
World J Surg; 5(5):769-771 1981

Initial results in 20 patients using an external magnetic obturator (Biotrol M) for colostomy closure are reported. Experiences were generally good, with some detachment, noise, and one case of allergic skin reaction. Biotrol M is compared with the stoma cap, mini bag, gauze, and air strip. (1 Ref)

25. FIVE YEAR SURVIVAL IN PATIENTS WITH CARCINOMA OF THE RECTUM TREATED BY ELECTROCOAGULATION.

Eisenstat TE, Deak ST, Rubin RJ, Salvati EP, Greco RS
1010 Park Ave., Plainfield, NJ, 07060
Am J Surg; 143(1):127-132 1982

Sixty-eight patients with rectal cancer treated by electrocoagulation are reviewed. All were followed up for a minimum of 5 years. The survival rate in patients with small exophytic cancers is greater than 70%. However, the recurrence rate after electrocoagulation is 40%. Electrocoagulation offers an alternative for the primary treatment of rectal cancer, particularly in older patients with small lesions. (Author abstract) (16 Refs)

26. ELECTROCOAGULATION IN THE TREATMENT OF RECTAL CANCER.

Delarue D, Grossetti D, Launois B
Clinique Chirurgicale, Centre Hospitalier Regional Hopital Pontchaillou, rue Henri-Le-Guillou, 35033 Rennes, France
Ann Chir; 35(10):870-872 1981

Electrocoagulation treatment (ET) of 14 patients with rectal cancer is reviewed. The av patient age was 72.5 yr. In all cases, ET was considered palliative treatment because age, medical complications or metastases had ruled out surgical treatment. The 14 patients in the series represented 7% of the 202 patients referred for surgical treatment of rectal cancer. Tumors were low-lying in all cases in order to be accessible to ET. In six cases, functional problems completely disappeared following ET, and in three patients, there was significant improvement with functional problems following ET. Postoperative complications included two cases of hemorrhage and one of incontinence leading to colostomy. The principal complication was tumor recurrence which occurred in five cases. Four patients underwent secondary ET treatment because of tumor recurrence. Deaths occurred in 11 cases with an av postoperative survival of 13.80 mo. In 2/3 cases, death was unrelated to cancer. Three patients were alive without recurrence at 10, 36, and 39 mo following ET. ET is recommended because of its simplicity, short hospitalization, and success in relieving functional disorders. (16 Refs) (In FRE)

27. PHASE II TRIAL OF COMBINATION THERAPY WITH CONTINUOUS-INFUSION PALA AND BOLUS-INJECTION 5-FU.

Weiss GR, Ervin TJ, Meshad MW, Kufe DW
Div. Medicine, Sidney Farber Cancer Inst., Harvard Medical Sch., 44 Binney St., Boston, MA, 02115
Cancer Treat Rep; 66(2):299-303 1982

Fifty-seven patients were treated with continuous infusion of phoshonoacetyl-L-aspartate (PALA) at a dose of 850 mg/m(2)/day x 5 and iv bolus injection of 5-fluorouracil (5-FU) at a dose of 300 mg/m(2)/day x 5, which was given at the end of each 24-hour PALA infusion; the treatment interval was 28 days. The overall response rate among 43 evaluable patients was 14%. Two of 21 patients (10%) with colorectal carcinoma, two of eight patients with pancreatic carcinoma, and two of four patients with breast carcinoma achieved partial responses lasting 2-12 months. One of the responding patients with colon cancer and two with breast cancer had failed to respond to prior therapy with 5-FU; one of the responding patients with breast cancer had previously received an inadequate trial of a similar regimen. Toxic effects were mild to moderate and were confined to oral mucositis in most patients. It is concluded that this regimen offers little enhancement of the antitumor activity of 5-FU in patients with colorectal cancer previously treated with 5-FU. Investigation of other infusion techniques for the PALA and 5-FU combination is recommended, with particular attention to the treatment of colorectal, pancreatic, and breast carcinomas. (Author abstract) (16 Refs)

28. PHASE II STUDY OF ANGUIDINE IN GASTROINTESTINAL MALIGNANCIES: A SOUTHWEST ONCOLOGY GROUP STUDY.

Bukowski R, Vaughn C, Bottomley R, Chen T
Southwest Oncology Group, Operations Office, 3500 Rainbow Blvd, Suite 100, Kansas City, KS, 66103
Cancer Treat Rep; 66(2):381-383 1982

The Southwest Oncology Group conducted a Phase II study of anguidine in 134 patients with gastrointestinal malignancies. Anguidine was administered as a 4-hour infusion at doses of 3.0 and 4.5 mg/m2 daily x 5. Response rates for patients with colon carcinoma were 22% (4 of 18 patients without previous chemotherapy) and 6% (4 of 63 patients with previous chemotherapy). There were no responses in patients with pancreatic cancer (4 patients) or gastric cancer (6). Toxic effects included thrombocytopenia (19.8%), leukopenia (18.8%), nausea and vomiting (49%), hypotension (37%), and confusion (12%). Antitumor activity of anguidine in patients with colon cancer may be similar to that of 5-FU, but nonhematologic toxicity is substantial. (Author abstract) (5 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

29. ELECTROMYOGRAPHIC EVIDENCE OF INFERIOR GLUTEAL NERVE COMPROMISE: AN EARLY REPRESENTATION OF RECURRENT COLORECTAL CARCINOMA.

LaBan MM, Meerschaert JR, Taylor RS
William Beaumont Hosp., William Beaumont Medical Building, Suite 703, 3535 West 13 Mile Road, Royal Oak, MI, 48072
Arch Phys Med Rehabil; 63(1):33-35 1982

Lumbosacral or primary buttock pain and cutaneous anesthesia in the distribution of the posterior femoral cutaneous nerve were the initial symptoms in five patients later proven to have extensions of previously resected colorectal malignancy. The initial electromyographic impression of an inferior gluteal nerve mononeuropathy associated with recurrent neoplasia was confirmed by a positive colon biopsy in one case and widespread pelvic metastasis demonstrated at laparotomy in the four remaining cases. Four of the five patients also had increased levels of carcinoembryonic antigen. Roentgenographs and other laboratory data were otherwise normal in all five cases. Entrapment of the inferior gluteal nerve and the accompanying posterior femoral cutaneous nerves is facilitated by its medial, intrapelvic fixation at its origin from the sciatic nerve and the crowding effect of the piriformis muscle above, the dorsal rim of the sciatic notch behind and the inferior gluteal vessels and nodes below. The demonstration of hypesthesia over the inferior lateral buttock and a concomitant history of colorectal malignancy should alert the examiner to the possible presence of an inferior gluteal nerve neuropathy. (Author abstract) (7 Refs)

30. THIRTEEN PRIMARY ADENOCARCINOMAS OF THE ILEUM AND APPENDIX: A CASE REPORT.

Wagner KM, Thompson J, Herlinger H, Caroline D
Surgical Pathology, Hosp. Univ. Pennsylvania, Box 527, Philadelphia, PA, 19104
Cancer; 49(4):797-801 1982

Adenocarcinomas of the ileum and appendix are uncommon. Multiple synchronous adenocarcinomas of the small bowel without carcinoid features are even more unusual, with only seven reported cases in the literature. The radiologic and pathologic findings are reported in a case with 13 separate, well-documented synchronous primary adenocarcinomas of the ileum and appendix. The value of the double-contrast small bowel enema is emphasized. (Author abstract) (7 Refs)

31. A REPORT ON A CASE OF REIFFERSCHEID'S PROCEDURE FOR TOTAL COLECTOMY IN THE MANAGEMENT OF GARDNER'S SYNDROME.

Canarelli JP, Vermynck JP, Dupas JL, Woestelandt T, Pietri J
Service de Chirurgie Pediatrique, Centre Hospitalier Universitaire d'Amiens, Place Victor-Pauchet, 8000 Amiens, France
Ann Chir; 35(10):842-845 1981

Gardner's syndrome was diagnosed and treated in a 12-yr-old child. Because of the risk of malignant degeneration of such cases, radical surgery is often required. Reifferscheid's procedure which preserves the rectal sphincter by ileo-rectal anastomosis was chosen because of the patient's age. The patient was able to eat on the 12th postsurgical day, and endoscopic examination 2 mo later revealed a good anastomosis. The advantage of the procedure consist in the postsurgical surveillance which is facilitated because of the area of the scar (6-8 cm from the rectum) beeing easily accessible by rectoscopy, and adenomas remaining after surgery can easily be removed. Such a procedure also eliminates the inclusion of polyps in the scar. The patient was able to lead a normal life with good continence, having from 1-2 stools/day. (22 Refs) (In FRE)

32. EFFECT OF A NEW BIFUNCTIONAL NITROSOUREIDO DERIVATIVE ON HUMAN COLORECTAL TUMOR XENOGRAFTS.

Kopper L, Lapis K, Csanyi E, Horvath T
1st Inst. Pathology and Experimental Cancer Res., Semmelweis Medical Univ., Budapest, Hungary
Anticancer Res; 1(4):229-233 1981

Tumor inhibiting effect of a bifunctional nitrosoureido derivative 1-[(2-chloroethyl)-3-nitrosoureido]-4-[3-(2 chloroethyl)-1-nitrosoureido]-1,4-dideoxy-D,L-threitol (GYKI-13324) was studied on four human colorectal tumor xenograft lines: HT 6 and HT 15 (adenomatous tumors), HT 3 and HT 22 (mucinous tumor). LD50 values on BDF1 mice were 80 mg/kg with ip and 135 mg/kg with po administration. The ip administration of GYKI-13324 and 1,3-bis(chloroethyl)-1-nitrosourea (BCNU) caused temporary tumor growth inhibition followed by regrowth of tumors at a rate similar to that of the controls. Po treatment with single dose administration produced a longer delay in tumor growth. Doses of 30 mg/kg BCNU and 50 mg/kg GYKI-13324 led to total regression of some tumors. When the dosage regime was interrupted by a 2 wk period, the tumor inhibiting effect decreased. Daily doses of 10 mg/kg GYKI-13324 for 5 subsequent days induced partially the same therapeutic effect as that in the case of a single large dose administration. Sensitivity of HT 15 line was high for single po application of 30 mg/kg BCNU and 50 mg/kg GYKI-13324, while the HT 22 and HT 3 lines showed less sensitivity. Results showed that GYKI-13324 is as effective as BCNU and less toxic, and GYKI-13324 appears to be the candidate for trials in the clinical management of colorectal tumors. (6 Refs)

33. RADIOLABELING OF MONOCLONAL ANTITUMOR ANTIBODIES: COMPARISON OF I-125 AND IN-111-ANTI-CEA WITH GA-67 IN A NUDE MOUSE-HUMAN COLON TUMOR MODEL (MEETING ABSTRACT).

Halpern SE, Stern PL, Hagan PL, Chen A, David GS, Desmond WJ, Adams TH, Bartholomew RM, Frincke JM, Brautigam CE
University of California, Veterans Administration Medical Center, San Diego, CA
Clin Nucl Med; 6(9S):453 1981

Monoclonal antitumor antibodies (MoAbs) labeled with I-131 have been shown to concentrate in murine tumors. Work in our own laboratory indicates that I-125-anti-carcinoembryonic antigen (CEA) MoAbs, while stable in vitro, dehalogenate in vivo. The purpose of the following study was to compare I-125 and In-111-anti-CEA MoAbs with Ga-67 in a nude mouse-human colon tumor model. Anti-CEA was labeled with I-125 using the Bolton-Hunter method, shown to be stable in saline at 37 C over a 72-hr period and to react with specific antigen to 70-80% efficiency. The antibody was conjugated with diethylenetriamine pentaacetic acid (DTPA) using DTPA anhydride, then labeled with In-111. The In-111-anti-CEA complex was stable in vitro with greater than 70% binding to CEA. Nude mice bearing human colon tumors were injected with similar quantities of both isotopes and sacrificed at 4, 24, 48 and 72 hr. Distribution and excretion studies were performed. Tissue concentrations were computed as % injected dose/gm (%ID/G). Peak tumor %ID/G occurred for I-125 (5%) at 4 hr, for In-111 (23%) at 72 hr, and for Ga-67 (5%) at 24 hr. Greater than 70% of the I-125 was excreted in the urine by 48 hr, compared to less than 10% of the In-111. Tumor/blood and muscle ratios for In-111-anti-CEA were 8:1 and 39:1 at 72 hr. In-111-anti-CEA MoAbs are superior to iodinated anti-CEA MoAb or Ga-67 as a potential tumor imaging agent and should be used preferentially if imaging studies are undertaken with radiolabelled MoAbs in humans. (no Refs)

34. MORPHOLOGICAL CHARACTERISTICS OF TUMOR EXPLANTS CULTURED IN THE DIFFUSION CHAMBERS.

Iakhimovich LV, Semenova-Kobzar' RA, Umanskii IuA
Dept. Immunology of Carcinogenesis, Inst. Problems in Oncology, Kiev, USSR
Tsitologiia; 23(11):1304-1308 1981

Kinetics of proliferation and morphological characteristics of human tumor explants cultured in the diffusion chambers were studied. Surgery specimens of squamous cell carcinoma of the esophagus, adenocarcinoma of the rectum bronchogenic adenocarcinoma of the lung, and squamous cell carcinoma of the lung were cultured in the diffusion chambers implanted into the abdominal cavity of mice for 3-21 days. Cytological examination of tumor explants showed progressive proliferation of both epithelial and fibroblastlike cells. Fibroblastlike cells were located in the center of the filter, while epithelial cells formed layers of various density near the edge of the filter. The rate of proliferation and the ratio of epithelial and fibroblastlike cells depended upon the type of the tumor. (18 Refs) (In RUS)

35. TROPHIC EFFECTS OF GASTRIN ON COLORECTAL NEOPLASMS IN THE RAT.

McGregor DB, Jones RD, Karlin DA, Romsdahl MM
Dept. Surgery, Univ. Nevada - Reno, 1000 Locust St., Reno, NV, 89520
Ann Surg; 195(2):219-223 1982

This study was designed to determine the effect of gastrin on colorectal neoplasms in the rat. Multiple colon and rectal cancers were induced in each of 57 rats with methylazoxymethanol. Animals were randomly assigned to groups: (1) antral exclusion, (2) antrectomy, (3) sham, or (4) sham with subsequent pentagastrin injections. Resulting tumors were analyzed for concentration and synthesis of DNA, RNA, and protein. The number of tumors per rat and distribution of tumors within the colons did not vary among groups. Antrectomy did not alter the gastrin level, and tumors developing in these animals did not differ from those of sham controls. Antral exclusion markedly raised serum gastrin levels. Both chronic endogenous hypergastrinemia and administration of exogenous pentagastrin significantly increased tumor synthesis and concentration of DNA, RNA, and protein. We conclude that gastrin exerts a trophic effect on colorectal neoplasms in rats. This biological phenomenon suggests a tumor regulatory role for the hormone. (Author abstract) (11 Refs)

36. SPONTANEOUS REGRESSION OF COLON CANCER IN HIGHLY INBRED WF RATS: GENETIC ANALYSIS.

Saeki K, Miyamoto M, Kitamura H, Hiroyoshi T
Dept. Pathology, Sch. Medicine, Osaka Univ., Osaka, Japan
Gan No Rinsho; 27(13):1623-1626 1981

The occurrence and spontaneous regression of colon cancers in inbred WF rat parents and offspring were studied. When dams of a non-cancer-bearing strain were crossed with males of cancer-bearing, spontaneous regression, or non-cancer-bearing strains, cancers developed in 21%, 14.1%, and 22.7% of the offspring, respectively; spontaneous regression occurred in 35%, 46.8%, and 23.5%, respectively. Results suggest two independent genetic factors, one carcinogenic and one regressive, governing phenotype. (10 Refs) (In JPN)

37. EFFECTS OF GLUCOCORTICOID HORMONES ON CELL PROLIFERATION IN DIMETHYLHYDRAZINE-INDUCED TUMOURS IN RAT COLON.

Tutton PJ, Barkla DH
Dept. Anatomy, Monash Univ., Clayton, Victoria, 3168, Australia
Virchows Arch [Cell Pathol]; 38(2):247-251 1981

Adrenocortical hormones have previously been shown to influence cell proliferation in many tissues. In this report, their influence on cell proliferation in the colonic crypt epithelium and in colonic adenocarcinomata is compared. Colonic tumor cell proliferation was found to be retarded following adrenalectomy and this retardation was reversible by administration of hydrocortisone, or by administration of synthetic steroids with predominantly glucocorticoid activity. Tumor cell proliferation in adrenalectomized rats was not promoted by the mineralocorticoid hormone aldosterone. Neither adrenalectomy, nor adrenocortical hormone treatment, significantly influenced colonic crypt cell proliferation. (Author abstract) (21 Refs)

38. EXPERIMENTAL COLON CARCINOGENESIS IS FACILITATED BY ENDOGENOUS FACTORS IN THE INTESTINAL CONTENTS.

Lewin MR, Ferulano GP, Cruse JP, Clark CG
Dept. Surgery, Univ. Coll. London, Rayne Inst., University St., London, WC1E 6JJ, England
Carcinogenesis; 2(12):1363-1366 1981

The theory that endogenous factors in the intestinal contents may be pathogenic during large bowel carcinogenesis was tested in the dimethylhydrazine (DMH)-induced rat colon cancer model. Thirty female Wistar rats, each serving as their own control, had a surgical transection of the proximal colon with reanastomosis to the rectum, therby excluding part of the colon from fecal contact. All rats then received a course of DMH (40 mg/kg body wt/wk sc for 10 weeks) while fed on Vivonex. This diet was selected because it lacks known exogenous (dietary) cocarcinogens. It also produces mucosal atrophy in functioning (proximal) colon, to parallel the disuse atrophy induced in the defunctioned (distal) colon. Animals remained on the diet throughout the experiment and were killed when moribund or at 40 weeks. At necropsy, the anatomical distribution, number, size and histological type of colon tumors were compared between functioning and defunctioned colonic segments within the same animal. At autopsy, there were significantly fewer colon tumors in the defunctioned segment (p less than 0.005). Furthermore, there were significantly fewer carcinomas (p less than 0.005) and fewer tumors greater than 1 cm diameter (p less than 0.01) in this segment. The data indicate that endogenous factors in the intestinal contents facilitate chemically-induced colon carcinogenesis. Luminal nutrition may be implicated. (Author abstract) (21 Refs)

39. ENZYMATIC, HEMATOLOGICAL AND HISTOLOGICAL STUDIES DURING CARCINOGENESIS OF THE LARGE INTESTINE IN RATS UNDER THE EFFECT OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE.

Przewlocki T, Chlap Z, Czosnek-Dabros E, Szot W
Zaklad Patofizjologii, Instytut Patologii AM, ul. Grzegorzecka 16, 31-531 Krakow, Poland
Patol Pol; 32(2):199-212 1981

The effects of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG; 0.25% aqueous soln) administered as an enema for 7 wk, on enzymatic, hematological and histological characteristics were studied in 64 female Wistar WAG rats during carcinogenesis. Thirty-six other rats served as untreated controls. MNNG did not cause any significant changes in the hematological parameters before the appearance of tumors, but cystic degeneration of the liver was seen in some animals. Changes in the activities of some plasma enzymes were found during the intensive development of the tumors of the colon. The gamma-glutamyl transpeptidase and aspartate transaminase activities increased, and the cholinesterase activity decreased compared with the controls. Among the hepatic enzymes, aspartate transaminase activity was increased in rats with hepatic cysts between wk 40-60. The alkaline phosphatase activities in the serum and liver showed no abnormal changes compared with the controls. The intensity of the enzymatic disturbances was correlated with the stage of development of the adenomas and adenocarcinomas of the colon. (43 Refs) (In POL)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

40. HEREDITARY COLON CANCER. IDENTIFYING THE HIGH-RISK PERSON.

Lynch HT, Lynch PM, Albano WA, Lynch JF
Dept. Preventive Medicine, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178
Consultant; 22(1):331,333-334,336-337,339,342-343 1982

Identification and management of hereditary colorectal cancer are described, with emphasis on surveillance and follow-up protocols developed for family members at high risk for the malignancy. Two major subtypes of hereditary colorectal cancer exist: those with and those without multiple adenomatous colonic polyps. Polyposis coli syndromes account for less than 1% of all colorectal cancers and include a spectrum of syndromes with and without extracolonic signs. Cutaneous and osseous tumors may be present in Gardner's syndrome; nervous system tumors may appear in Turcot syndrome. Identification of a patient affected with familial polyposis coli is important; the disease is associated with an easily identifiable biological marker, polyps, that precedes malignant change. An expected one of the patient's parents, one-half of his siblings, and one-half of his children may be similarly affected. The polyposis phenotype is usually first expressed in the rectosigmoid area by the second decade, years before cancer occurs. Family surveillance, a protocol for diagnosis and management of hereditary colon cancer, and the physician's responsibility are discussed. (5 Refs)

41. THE PREVALENCE OF POLYPS OF THE LARGE INTESTINE IN OSLO: AN AUTOPSY STUDY.

Vatn MH, Stalsberg H
Rikshopitalet, Oslo 1, Norway
Cancer; 49(4):819-825 1982

The colon and rectum were removed from 445 consecutive autopsies and examined for the presence of polypoid lesions under an illuminating magnifying lens. There were seven clinically undiagnosed carcinomas, 329 adenomas, 174 hyperplastic polyps, 59 mucosal tags, 34 other polypoid lesions, and 54 polyps in which no histologic diagnosis could be made. Adenomas were present in 34% of the men and 32% of the women. The adenoma prevalence rate increased smoothly with age in men, whereas the rate in women showed a biphasic variation with a peak at 50-59 years followed by a second increase after 70 years of age. The distribution of adenomas within the bowel showed a marked change with age, from a moderate left-sided predominance before 60 years of age to a marked right-sided predominance in patients over 80 years of age, particularly in men. Hyperplastic polyps were present in 27% of the men and 18% of the women. In men, their frequency and distribution within the bowel showed similar changes with age as were seen for the adenomas. In women, no such age-dependency was observed for hyperplastic polyps. Multiplicity of polyps increased with age and was more pronounced in men than in women. Adenomas in women tended to be larger, more atypical, and more villous than in men. A comparison with a similar study from Northern Norway showed no difference in the prevalence of adenomas in spite of a 70% higher incidence rate for colorectal cancer in Oslo. (Author abstract) (23 Refs)

42. CANCER INCIDENCE IN JAPAN, 1975: CANCER REGISTRY STATISTICS.

Fujimoto I, Hanai A, Aoki K, Sugenoya J, Ohno Y, Kobayashi H, Kawaguchi T
Dept. Field Res., Center for Adult Diseases, Osaka, Nakamichi-1-3-3, Higashinari-ku, Osaka 537, Japan
Gann Monogr Cancer Res; 26:92-120 1981

Cancer incidence statistics for 1974-1977 were compiled and edited based on data collected by the Research Group for Population-based Cancer Registration in Japan, and cover 13 prefectures and 2 cities including a total of 47.5 million persons, corresponding to 43% of the Japanese population. The following statistics are included: number of new cases, and incidence rates by sex and site for each registry; estimated cancer incidence by age, sex, and site for Japan, 1975; av annual incidence rates for cancer by site in Osaka, 1967-1976; and trends in age-adjusted incidence rates by sex and four-digit site in Osaka, 1963-1977. An appendix includes estimates of point prevalence of cancer for the second Wednesday in July, 1977, by site, age, and sex for all patients treated in 1/10th of all hospitals and 1/100th of clinics and dispensaries randomly selected throughout Japan. (8 Refs)

43. INCIDENCE OF MALIGNANT NEOPLASMS OF DIGESTIVE ORGANS.

Zemla B, Kolosza Z, Czech J, Jamrozik W
Instytut Onkologii, ul. Wybrzeze Armii Czerwonej 15, 44-101 Gliwice, Poland
Wiad Lek; 34(13):1077-1083 1981

Epidemiological data on the incidence of malignant neoplasms of the digestive organs in the population of Zabrze and its suburbs between 1965-1975 are presented. Malignant neoplasms of digestive organs were diagnosed in 199 men and 205 women. Esophageal tumors were diagnosed in 6 men and 4 women, gastric tumors in 130 men and 71 women, colon tumors in 14 men and 41 women, rectal tumors in 11 men and 23 women, hepatic tumors in 11 men and 20 women, gallbladder tumors in 5 men and 23 women, and tumors of the pancreas, peritoneum and undetermined localizations in 20 men and 27 women. The standardized incidences per 100,000 population were 1.64 for esophageal tumors, 32.96 for gastric tumors, 3.45 for colon tumors, 2.86 for rectal tumors, 2.81 for hepatic tumors and 50.96 for all localizations in men. The corresponding incidences in women were 0.30, 11.10, 6.54, 3.60, 3.07 and 32.03. The incidence of malignant tumors of the digestive organs, especially of the stomach, was significantly lower in the autochthonous populations of districts supplied with water of relatively high hardness, ie, with high levels of magnesium salts, chlorides and sulfates, than in the immigrant population. (8 Refs) (In POL)

44. DIET AND CANCER OF THE LARGE BOWEL.

Zaridze DG
Analytical Epidemiology Programme, Div. Epidemiology and Biostatistics, International Agency for Res. on Cancer, 150 Cours Albert Thomas, 69372 Lyon, Cedex 2, France
Nutr Cancer; 2(4):241-249 1981

Suspected etiological and protective factors in large bowel cancer are reviewed. Incidence of large bowel cancer correlates with consumption of fat, protein or meat. Etiological hypotheses propose that high-fat diet is related to an increased risk of large bowel cancer, while analysis of the geographical distribution of colon cancer in humans. The results of further epidemiological studies do not unequivocally support the hypotheses. Control studies do not confirm an association between diet and the colorectal cancer risk at the individual level. Lack of uniformity among the findings of epidemiological studies concerned with the role of diet could be explained by lack of sensitive and reproducible methods for assessment of diet in epidemiological studies and lack of knowledge of the mode of action of dietary factors responsible either for the development of the tumor or for protection against it. Research on large bowel cancer in humans is focused on the promoting factors. Initiators could be the factors responsible for the individual risk for colon cancer in populations with homogeneous high-fat diet practices. Available data indicate adenomatous polyps and non-invasive carcinoma of the large bowel could remain stationary. Future epidemiological research on diet and large bowel cancer should deal with more precisely defined hypotheses in which the multifactorial nature of the tumor would be taken into account. (49 Refs)

45. IS COLON CANCER A DISEASE OF CIVILIZATION?.

Raiser MW
Div. Gastroenterology, Edgewater Hosp., 5700 N. Ashland Ave., Chicago, IL, 60660
Minerva Dietol Gastroenterol; 27(4):638-640 1981

Epidemiology of carcinoma of the colon (CC) is discussed. CC has become increasingly common in North America and Western Europe in the last 30 yr. These areas have higher income, a higher standard of living, and higher meat consumption. A diet rich in meat and associated animal fat increases the production of cholic acids. Feces have higher amounts of cholic acids and their degradation products, some of which are carcinogens. Constipation, another problem associated with a higher standard of living, increases the amount of time feces are in contact with intestinal walls. Japanese, Poles, and other Eastern Europeans, all from areas that are low in CC, become as prone to CC as the rest of the population after emigration to the United States. On the other hand, Seven Day Adventists living in Loma Linda, California and consuming vegetarian diets have a much lower CC rate than the rest of the population; the amount of cholic acids and their derivatives in their feces is much lower. Another factor associated with diet is the type of bacterial flora and enzymes active in the intestines (beta-glucuronidase, nitroreductase, azoreductase etc). Associated with these problems is increased intestinal diverticulosis. Current dietary recommendations are for decreased total calories, animal fat, and cholesterol, and increased vegetable fibers and unsaturated fats. (14 Refs) (In ITA)

46. SHOULD WE EAT MORE FIBRE?

Stephen AM
Dunn Clinical Nutrition Centre, Addenbrookes Hosp., Trumpington St., Cambridge CB2 1QE, England
J Hum Nutr; 35(6):403-414 1981

Various aspects of the role of dietary fiber in health are discussed: epidemiological studies, effects of fiber on fecal weight, diverticular disease, colon cancer, ischemic heart disease, and the possibility of the recommendation of a standard fiber intake. Outline of a diet fed to volunteers, containing 40 g dietary fiber/day, is presented. The type of fiber to be recommended is discussed. (62 Refs)

47. NUTRITION AND CANCER. INTRODUCTORY REMARKS.

Carroll KK
Univ. Western Ontario, Ontario, Canada
Nutr Cancer; 2(4):197-198 1981

Food consumption data, methods of food analysis, animal models, recommendations regarding cancer at specific sites (colon, breast, stomach, other sites), and data on cancer incidence and mortality have been reviewed. No dietary recommendations to the public have been made. Further experiments are needed to clarify the role of diet in carcinogenesis. (no Refs)

48. WORLD CANCER MORTALITY.

Segi M, Aoki K, Kurihara M, Tominaga S, Kuroishi T
Segi Inst. Cancer Epidemiology, Yomei-cho 2-5, Mizuho-ku, Nagoya 467, Japan
Gann Monogr Cancer Res; 26:121-274 1981

Cancer mortality data for 56 countries are presented based on original compilation, calculation, and editing of statistics of individual countries, or that compiled by the World Health Organization and United Nations. The following statistics are included: age-adjusted death rates from cancer by site in 1950-1967 and in 1970-1975, including figures illustrating comparative incidences in 1975; number of deaths from all cancers and sex- and age-specific death rates by site in 1975; cumulative death rates from cancer by sex, 0-74 yr, for selected sites in selected countries in 1954-1955 and 1974, and the ratio of the rates in 1974 to those in 1954-55; estimated population in 1975, mean or mid-yr, general mortality, infant mortality, and proportion of deaths from neoplasm in all causes of deaths in 1975; and populations by sex and age around 1975 in all 56 countries. An appendix provides age-adjusted death rates for cancer by site in 50 countries for the yr 1975. (12 Refs)

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. EVALUATION OF RAPID COLONOSCOPY PREPARATION USING A NEW GUT LAVAGE SOLUTION.

Goldman J, Reichelderfer M
(c/o Reichelderfer), William S. Middleton Memorial Veterans Admin Hosp., 2500 Overlook Terrace, Madison, WI, 53706
Gastrointest Endosc; 28(1):9-11 1982

The traditional colonoscopy preparation of laxatives and enemas requires 2 days to complete and is occasionally unsatisfactory. The alternative method, gut lavage with saline-based solutions, is hazardous in elderly or compromised patients because of overhydration. We studied a new, orally ingested

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electrolyte solution containing sodium sulfate and polyethylene glycol as preparation for elective colonoscopy in a consecutive series of 43 patients. Almost all patients achieved a good to excellent preparation. There were no changes in fluid or electrolyte balance and no complications of the procedure. Colonoscopy preparation with this technique is rapid, effective, and well tolerated and is a safe alternative to the standard approach. (Author abstract) (16 Refs)

2. CASTOR OIL OR SENNA PREPARATION BEFORE COLONOSCOPY FOR INACTIVE CHRONIC ULCERATIVE COLITIS.

Gould SR, Williams CB
(c/o Williams), St. Mark's Hosp., London, England
Gastrointest Endosc; 28(1):6-8 1982

Few clinically apparent clinical relapses of colitis occurred in 340 patients with previously extensive ulcerative colitis in an inactive phase submitted to total colonoscopy for dysplasia screening after bowel preparation with castor oil or senna. A prospective trial in 46 such patients showed both preparations to be equally safe and effective. Minor untreated disturbances of bowel habit occurred in 14 patients (30%), and 3 patients (7%) required a short period of oral corticosteroids. No patients with inactive colitis in either the retrospective series or the trial group had a serious exacerbation of colitis as a result of the bowel preparation, which was considered necessary and clinically justified for the purposes of cancer screening. (Author abstract) (7 Refs)

3. TOTAL COLONOSCOPY IN CHILDREN.

Williams CB, Laage NJ, Campbell CA, Douglas JR, Walker-Smith JA, Booth IW, Harries JT
Endoscopy Unit, St. Mark's Hosp., City Road, London EC1V 2PS, England
Arch Dis Child; 57(1):49-53 1982

One hundred and twenty-three total colonoscopies were performed on 115 children with ages ranging from 3 mo to 16 yr. The major indications were suspected inflammatory bowel disease and unexplained rectal bleeding. Ninety-seven percent of all procedures were carried out with sedation only. Adult colonoscopes were used in most of the patients but in babies and small children pediatric instruments were preferable. Total colonoscopy was possible in all patients with a patent colon. The terminal ileum was examined in 63 patients. Endoscopic snare polypectomy was successfully carried out in eight children and multiple hemangiomas were electrocoagulated in one. Total colonoscopy in this pediatric series proved to be at least as easy, rapid, well-tolerated, and safe as in adults. In selected patients a single colonoscopy can give an accurate diagnosis with biopsy proof and sometimes the opportunity for definitive treatment. (Author abstract) (31 Refs)

4. ENDOSCOPIC STUDY OF MINUTE PROTRUDING LESIONS IN THE RECTUM USING A DYE-ABSORPTION DISTRIBUTION METHOD.

Nakajima T, Tsuboi M, Wada J, Ueno K, Ishikawa M
Second Dept. Internal Medicine, Yamagata Univ. Sch. Medicine, Yamagata Pref., Japan
Gastroenterol Endosc; 23(2):248-252 1981

Indigo carmine dye (0.13% soln) was sprayed in the rectal lumen of 217 patients (107 men, 110 women; 17-78 yr old) during the second phase of rectosigmoidoscopy. The patients had complaints of diarrhea or lower abdominal discomfort. The dye-rectosigmoidoscopy was used to detect polyps or cancers less than 5 mm in diameter. Minute protruding lesions were observed in 64/217 patients. The lesions were solitary in 43 cases and multiple in 21. Histological examination of biopsy specimens of the protruding lesions showed that 9 were tubular adenomas, all of which were solitary lesions, 15 were metaplastic polyps, 15 were definitive or suspected metaplastic polyps, and 39 were lesions that originated in the rectal mucosa but had no clear origin. One biopsy specimen showed a scattering of small polypoid lesions with areas of adenocarcinoma; this was confirmed at autopsy to be a metastatic gastric cancer of the rectal mucosa. The dye-spraying method, used in conjunction with rectosigmoidoscopy, was useful for detecting small protruding lesions showing inflammatory scar patterns. (13 Refs) (In JPN)

5. POSTOPERATIVE SURVEILLANCE OF COLORECTAL CARCINOMA.

Nava HR, Pagana TJ
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Cancer; 49(5):1043-1047 1982

Two-hundred-forty patients with previously resected colorectal carcinoma were investigated for neoplasia at 6 mo, 12 mo and then at yearly intervals during a 4-yr period. Physical examination, occult blood, rigid sigmoidoscopy, barium enema and colonoscopy were used during the surveillance. Out of 304 colonoscopies, 68 were positive for neoplasia, 11 metachronous, and 17 recurrent cancers with 66 tubular adenomas and nine villous adenomas were found. Barium enema detected 38% of the lesions. Occult blood in stool was positive in 18.5%. The results of the methods of surveillance are analyzed and the relative value of each method is discussed. (Author abstract) (20 Refs)

6. DIMINUTIVE POLYPS: HISTOPATHOLOGY, SPATIAL DISTRIBUTION, AND CLINICAL SIGNIFICANCE.

Tedesco FJ, Hendrix JC, Pickens CA, Brady PG, Mills LR
Section Gastroenterology, Dept. Medicine, Medical Coll. Georgia, Augusta, GA, 30912
Gastrointest Endosc; 28(1):1-5 1982

This retrospective study of 329 diminutive colon polyps revealed that 49.2% of the polyps were neoplastic, whereas 49.9% were nonneoplastic. 36.8% of the polyps were metaplastic, and 0.9% had mixed metaplastic and adenomatous components. The metaplastic polyps had a predominance in the distal portion of the large bowel, with 76.9% being located distal from the splenic flexure and 52.9% being located in the rectosigmoid area. Neoplastic polyps were distributed throughout the colon, with 65.4% located from the splenic flexure distally and 34.5% located proximal to the splenic flexure. These findings suggest that a much larger proportion of diminutive polyps are neoplastic and therefore at risk to progress of carcinoma than previously considered. (Author abstract) (13 Refs)

7. ARGYROPHIL CELLS IN ADENOMAS OF FAMILIAL POLYPOSIS COLI.

Okayasu I, Hatakeyama S, Iwama T, Utsunomiya J
First Dept. Pathology, Sch. Medicine, Tokyo Medical and Dental Univ., Tokyo, Japan
Bull Tokyo Med Dent Univ; 28(1):1-5 1981

The distribution of argyrophilic (ARG) cells in colonic mucosa was studied in resected ascending and sigmoid colon specimens from 15 patients (20-53 yr old) with familial polyposis coli (FPC: 12/15 patients belonged to 4 families) and uninvolved colonic mucosa from 5 control patients (28-70 yr old) with colonic adenocarcinomas unrelated to FPC. In the normal mucosa from FPC patients and controls and in the FPC adenomas, the frequency of ARG cells was significantly higher in the sigmoid colon than in the ascending colon. Scattered ARG cells were found in some of the FPC adenomas (especially of the sigmoid colon), but at a much lower frequency than in the nontumorous mucosa. ARG cells were found only in adenomas showing slight dysplasia and never in adenomas with moderate or severe dysplasia. Sigmoid adenomas from 6/15 FPC patients contained at least 10 ARG cells/adenoma. Three of the patients belonged to one family (represented by five members of the FPC group), suggesting that a gene related to the appearance of many ARG cells in FPC adenomas may be involved. Foci and ARG cells were observed in some FPC adenomas of the sigmoid colon (never the ascending colon), suggesting that the ARG cells might actively participate in growth of these tumors. (8 Refs)

8. THE RELEVANCE OF THE HISTOCHEMISTRY OF COLONIC MUCINS BASED UPON THEIR PAS REACTIVITY.

Culling CF, Reid PE, Dunn WL, Freeman HJ
Dept. Pathology, Faculty Medicine, Univ. British Columbia, Vancouver, British Columbia V6T 1W5, Canada
Histochem J; 13(6):889-903 1981

Histochemical methods for the study of epithelial mucins of the gastrointestinal tract, clinical application of this methodology, identification of metastases from colorectal adenocarcinomas, and changes noted in colorectal cancer and other pathological states are discussed. The histochemical data presented are used to justify the use of such histochemistry in the detection of early malignant change in colorectal epithelial cells. (57 Refs)

9. MUCIN HISTOCHEMISTRY OF THE ANAL CANAL EPITHELIUM. STUDIES OF NORMAL ANAL MUCOSA AND MUCOSA ADJACENT TO CARCINOMA.

Fenger C, Filipe MI
Dept. Pathology, Hvidovre Hosp., Univ. Copenhagen, Kettegard Alle 30, 2650 Hvidovre, Denmark
Histochem J; 13(6):921-930 1981

Colonic mucus from 39 specimens of anal canals from abdominal perineal resection s for carcinomas of the anal canal and rectum was studied histochemically. The patients included 32 with adenocarcinoma (25 men, 7 women: 44-81 yr old), 4 with squamous carcinoma (2 men, 2 women: 61-82 yr old), 2 with basaloid carcinoma (women: 51 and 78 yr old), and a women (age 81) with malignant melanoma. Tumors were in different stages (Duke classification) and degrees of differentiation. The adenocarcinomas were located at various distances (1-15 cm) from the dentate line. A mixture of sulfo- and sialomucins with scarcity or absence of O-acylated sialic acids found in the anal transition zone (ATZ) was similar to that in anal glands. Carcinomas located near the dentate line showed changes in mucin composition similar to those of the adjoining anal canal epithelium, regardless of tumor type. In colorectal mucosa, the mucins consisted of increasing amounts of sulfomucins with predominance of N-acyl derivatives, and in the anal glands of increasing amounts of sulfomucins and O-acyl derivatives of sialomucins. No changes were detected in the ATZ epithelium; no relationship could be established between mucin secretion and tumor type or distance above the dentate line. It is concluded, that while rectal and anal glands in the anal canal are exposed to stimuli which alter glycoprotein synthesis and secretion, these change are secondary to tumor growth and independent of histological type of tumor. (21 Refs)

10. A CANCER-ASSOCIATED MUCIN ALTERATION IN BENIGN COLONIC POLYPS.

Boland CR, Montgomery CK, Kim YS
Gastrointestinal Res. Lab., Veterans Admin. Medical Center, 4150 Clement St. (151-M2), San Francisco, CA, 94121
Gastroenterology; 82(4):664-672 1982

We have recently reported that the mucin in colon cancer is different from that in the normal colon, and this difference may be detected by selective lectin binding characteristics. The lectin Dolichos biflorus agglutinin (DBA) avidly binds to the mucin found in well-differentiated goblet cells in the normal colon, but does not bind to that in the majority of colonic cancers. Conversely, the lectin peanut agglutinin (PNA) does not bind to the mucin from the normal colon, but avidly binds to that in colon cancer. Therefore, these two lectins were used to determine if cancer-associated mucin were present in benign colonic polyps. Fluorescein isothiocyanate (FITC) conjugates of Dolichos biflorus agglutinin and peanut agglutinin were applied to fixed, unstained tissue sections of 56 colonic polyps and examined by fluorescent microscopy. Focal areas were found within the polyps in which FITC-DBA labeling was diminished (compared with the normal colon) and labeling with FITC-PNA appeared. The findings are expressed as the percentage of glands per polyp labeled by FITC-PNA. The median labeling in 31 benign tubular adenomas was 7% of the glands per polyp . In 16 benign tubular adenomas less than or equal to 7 mm in diameter, only 2% of the glands per polyp were labeled, while in 15 benign tubular adenomas greater than 7 mm in diameter, 24% of the glands per polyp were labeled. Carcinoma in situ or invasive carcinoma was found in nine adenomatous polyps, in which 41% of the adenomatous glands were labeled by FITC-PNA. Unexpectedly, in eight hyperplastic polyps, 89% of the glands were labeled by FITC-PNA. These results indicate that among neoplastic colonic polyps, cancer-associated mucin changes are present and are more widespread in larger tubular adenomas, villoglandular adenomas, and adenomas containing cancer. The presence of mucin that is bound by FITC-PNA may be an indication of an increased risk of developing cancer within a colonic polyp. The finding of the cancer-associated mucin in hyperplastic polyps raises new questions about pathogenesis of these benign, apparently nonneoplastic lesions. (Author abstract) (27 Refs)

11. CLINICAL AND HISTOLOGICAL STUDIES ON WHITE SPOTS OF COLONIC MUCOSA AROUND COLONIC POLYPS WITH SPECIAL REFERENCE TO THEIR ASSOCIATION WITH EARLY STAGE CANCER.

Muto T, Kamiya J, Sawada T, Sugihara K, Kusama S
First Dept. Surgery, Tokyo Univ. Sch. Medicine, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan
Gastroenterol Endosc; 23(2):241-247 1981

Of 21 early stage (mucosal and submucosal) large intestinal cancers that were obtained by endoscopic polypectomy, 7 were observed to have white spots in the mucosal area surrounding the cancer. During the same period, such white spots were not observed to be associated with any benign adenomas of the large intestine which were treated with polypectomy. Histologically, the white spots were composed of foamy cells that were just below the surface epithelium and between tubules and contained granules which were faintly staining with hematoxylin-eosin. The foamy cells were positive for PAS, alcian blue, mucicarmine and toluidine blue and were negative for oil red O. Examination of the foamy cells with electron microscopy showed that the granules in the cytoplasm of the foamy cells were without electron-density. The white spots were observed in the tissue surrounding advanced cancers of the large intestine as well. The white spots were thought to be useful in the diagnosis of elevated type early stage cancers of the large intestine. (5 Refs) (In JPN)

12. ULTRASTRUCTURE OF COLONIC POLYPS. II. LEUCHTENBERGER'S INCLUSION BODIES.

Balazs M, Csermely A
Karbonctani Osztaly, Fovarosi Tanacs Janos Korhaza, Diosarok ut. 1, Budapest 1125, Hungary
Morphol Igazsagugyi Orv Sz; 21(4):250-257 1981

Leuchtenberger's inclusion bodies (LIB) in colonic polyps were studied by electron microscopy. Development of LIB could be the result of membrane impairment caused by cell proliferation and changes in undifferentiated epithelial cells of the colonic mucosa. Increased frequency of LIB is apparently an important characteristic of malignant transformation. (10 Refs) (In HUN)

13. ADENOMATOUS AND CARCINOMATOUS CHANGES IN HAMARTOMATOUS POLYPS OF THE SMALL INTESTINE (PEUTZ-JEGHERS SYNDROME): REPORT OF A CASE AND REVIEW OF THE LITERATURE.

Perzin KH, Bridge MF
Div. Surgical Pathology, Columbia Univ., Coll. Physicians and Surgeons, 630 West 168th St., New York, NY, 10032
Cancer; 49(5):971-983 1982

The authors report the unique case of a patient with the Peutz-Jeghers (P-J) syndrome who had multiple small bowel hamartomatous polyps, some of which also showed adenomatous and carcinomatous changes. Over the course of 30 yr, over 100 small bowel and colonic polyps were resected; all histologically demonstrated the typical features seen in hamartomatous polyps. Several jejunoileal polyps excised during the last few mo of the patient's life showed not only hamartomatous features but also adenomatous epithelium. As far as the authors can determine, this is the first documented case of adenomatous changes found within a small bowel hamartomatous polyp. In addition, at least one duodenal polyp demonstrated areas of hamartoma, adenoma, and in situ carcinoma. The literature on the occurrence of gastrointestinal adenomas and carcinomas in patients with the P-J syndrome is reviewed, and the relationship of hamartomas, adenomas, and carcinomas of the gastrointestinal tract is discussed. (Author abstract) (83 Refs)

14. CLINICAL SIGNIFICANCE OF THE PREOPERATIVE PLASMA CARCINOEMBRYONIC ANTIGEN (CEA) LEVEL IN PATIENTS WITH CARCINOMA OF THE LARGE BOWEL.

Blake KE, Dalbow MH, Concannon JP, Hodgson SE, Brodmerkel GJ, Panahandeh AH, Zimmerman K, Headings JJ
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Dis Colon Rectum; 25(1):24-32 1982

Preoperative levels of perchloric acid extractable plasma CEA were measured in 911 patients with complaints of the digestive system. A final diagnosis of benign disease was made for 579 patients; 332 patients were found to have cancer. Data for the preoperative CEA values were examined for clinical significance as an aide to diagnosis, preoperative disease staging, and prognosis. The results of our analysis support the conclusions of many investigators that the CEA assay is not a clinically useful diagnostic test, but it shows limited value in preoperative staging and a somewhat stronger correlation with prognosis. (Author abstract) (78 Refs)

15. PREDICTIVE VALUE OF PLASMA CEA LEVELS: PREOPERATIVE PROGNOSIS AND POSTOPERATIVE MONITORING OF PATIENTS WITH COLORECTAL CARCINOMA.

Szymendera JJ, Nowacki MP, Szawlowski AW, Kaminska JA
Inst. Oncology, P.O. Box 47, PL-00973 Warsaw 22, Poland
Dis Colon Rectum; 25(1):46-52 1982

Plasma CEA levels were determined in 280 patients with histologically proven colorectal carcinoma: in 180 once or twice preoperatively and repeatedly postoperatively, and in 100 postoperative only. Preoperative levels correlated directly with surgical-pathologic state and inversely with the time of recurrence; ie, groups of patients with more advanced stage showed higher proportion of elevated CEA levels, and patients with higher levels had recurrences earlier. Levels above 20 ng/ml were strongly suggestive of liver metastases or disseminated disease. Postoperative plasma CEA levels displayed three patterns of variation. (1) Levels fluctuating within normal range, below 3.2 ng/ml, strongly evidenced that surgery was effective, and (2) those fluctuating below 7.5 ng/ml indicated usually nonmalignant concomitant disease; in either group no more than 10% of the patients had recurrences. (3) Levels rising persistently from a postoperative nadir indicated recurrence or, when the rise was dramatic, liver metastases or disseminated cancer in at least 97% of the patients. (Author abstract) (31 Refs)

16. IMMUNOLOGICAL COMPARISON OF OVARIAN AND COLONIC CEA.

Burtin P, Lamerz R, Gendron MC, Maunoury MT, Schnabel G
Institut de Recherches scientifiques sur le Cancer, BP 8-94802 Villejuif, France
Immunol Lett; 4(2):87-91 1982

Carcinoembryonic antigen (CEA) prepared from liver metastases of colon carcinomas (3 samples from 2 different livers) and from the ovary (2 from carcinomas, 2 from benign cysts) were compared immunologically by means of antisera prepared against each of them in rabbits. The Ouchterlony immunodiffusion technique showed the two antisera were identical. Radioimmunological experiments showed slight differences between some, but not all, ovarian and colonic CEAs and between individual preparations of colonic CEA. No organ specificity could be demonstrated for ovarian CEA. Ovarian cancer sera were assayed for CEA using both radioimmunoassay systems: anti-colonic CEA serum and colonic CEA as tracer, and anti-ovarian CEA serum and ovarian CEA as tracer. The values given by the two assays were highly correlated (rs = 0.8107, p less than 0.001), meaning that an organ specific assay for ovarian CEA is not needed. (8 Refs)

17. HUMAN COLON TUMOR ANTIGENS.

Yeoman LC, Taylor CW, Chakrabarty S

Nuclear Protein Lab., Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030

Methods Cancer Res; 19:233-271 1982

Colon cancer marker biology, cellular fractionation and antibody preparation, radioimmunoelectrophoresis, immunolocalization of GW-39 hamster colon tumor antigens, and purification and properties of colon antigens are reviewed. Subcellular fractionation of GW-39 colon adenocarcinoma cells into cytoplasmic and nuclear fractions yielded extracted antigens, which may have been dominated by other molecules when presented to a xenogeneic host as a group. Three potential antigen markers have been detected which share no immunological cross-reactivity with carcinoembryonic antigen. One of these, antigen 3, a glycoprotein of approx 150,000 mol wt, is most highly purified and characterized to date. Cancer marker molecules aid in the investigation of the biological mechanism involved in tumor promotion, carcinogenesis, or maintenance of cancer phenotype. (91 Refs)

18. PREDICTIVE VALUE OF TUBE LEUKOCYTE ADHERENCE INHIBITION (LAI) ASSAY FOR BREAST, COLORECTAL, STOMACH AND PANCREATIC CANCER.

MacFarlane JK, Thomson DM, Phelan K, Shenouda G, Scanzano R

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Cancer; 49(6):1185-1193 1982

The tube LAI assay measures accurately antitumor immunity in patients with early cancer but fails to detect up to 75% of patients with advanced cancer due to excess circulating organ-specific neoantigen (OSN). Substances such as prostaglandin E2 (PGE2) or aminophylline which increase intracellular nucleotides in leukocytes of patients with advanced cancer reversed this nonreactivity and greatly increased the sensitivity of the assay without any loss of specificity. Antitumor immunity can now be detected in advanced cancer, and a combination of the two assays gives prognostic potential to the assay: a positive test with PGE2 and negative test without indicates the patient has a large tumor burden. The specificity of the assay for each cancer was high and in most instances was greater than or equal to 95%. The PGE2 stimulated assay retained the high specificity. The sensitivity of the regular tube assay was often low, 33-56% because of the many advanced cancer patients tested, whereas the PGE2 stimulated assay showed almost a two-fold increase in sensitivity, 67-93%. The diagnostic value of the assay was estimated by calculating the predictive value for different prevalences of cancer. It was found that at low prevalences of cancer as found in the general population, the assay had a low diagnostic value since few patients with a positive test would have the cancer tested for. With prevalences of cancer of 5% or greater as might be found in a tertiary care clinical setting, the assay would seem to have diagnostic value since one half or more patients with a positive test would have the cancer tested for. Most false positives, but not all, are found in patients who have lesions that are often considered to increase their risk for cancer: severe dysplasia of breast, colon adenomas, chronic atrophic gastritis ad chronic pancreatitis, suggesting that the assay predicts oncogenesis. (Author abstract) (35 Refs)

19. SPECIFIC AND NON-SPECIFIC LYMPHOCYTE CYTOTOXICITY IN COLON CARCINOMA.

Vose BM, Gallagher P, Moore M, Schofield PF

Dept. Immunology, Paterson Lab., Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, Eng

Br J Cancer; 44(6):846-855 1981

The cytotoxic activity of peripheral-blood (PBL), lymphnode (LNC) and tumor-infiltrating lymphocytes (TIL) from 47 patients undergoing surgery for colon carcinoma (Duke's Stage A, 1 patients; B, 24; C, 15 and C with metastases, 7) was examined in short-term 51Cr-release assays, against fresh autologous tumor cells, allogeneic colon cancer cells and the erythroleukemia cell line, K562. Cytotoxicity against autologous cells was detected in at least one effector population in 23/47 patients (49%), with overall frequencies which did not differ for patients in different Duke's stages of disease. By contrast, lysis of allogeneic tumor cells was infrequent (11%) regardless of the effector population to which they were exposed. Cytotoxicity against K562, cells highly sensitive to NK activity, though variable, was detected in 93% of PBL of normal donors and 83% of patients, and among the latter showed no evidence of significant decline with advancing disease. However, LNC and TIL anti-K562 activity was infrequent (17%) in concordance with previous reports. There was no correlation between the ability of patients' PBL to lyse autologous tumor and K562 cells. The independence of these two cytotoxic actions was further explored in studies fractionating lymphocytes: autologous tumor killing was augmented in T-enriched PBL; whereas the greatest anti-K562 activity was found in the corresponding non-T fraction. Lymphocyte cytotoxicity in colonic neoplasia is thus manifest in two apparently independent lymphocyte populations; a relatively specific killer T-cell population, detectable in PBL, LNC and TIL, which is preferentially reactive with the autologous cells; and a non-specific killer population, largely limited to PBL, with the properties of NK cells. The activity of neither population reflects the clinical status of patients with this disease. (Author abstract) (28 Refs)

20. IMMUNOPEROXIDASE STUDY OF THE SECRETORY IMMUNOGLOBULIN SYSTEM IN COLONIC NEOPLASIA.

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J Clin Pathol; 35(1):14-25 1982

The relation of the secretory immunoglobulin system in the colon to colorectal cancer and dysplasia has been examined by staining routine formalin-fixed, paraffin-embedded sections from cases of carcinoma, adenoma and ulcerative colitis for secretory component (SC), IgA and J chain. In carcinomas there was a close relation between SC synthesis and differentiation and a similar relation was apparent between SC synthesis and degrees of dysplasia in adenomas. In both morphological and functional (SC synthesis) terms degree of dysplasia in adenomas resembled degrees of differentiation in carcinomas suggesting that the essential 'switch' in the progression towards neoplasia may occur at the level of the adenoma and that invasive malignancy can arise from dysplastic mucosa of varying severity. Actively regenerating mucosa in ulcerative colitis (UC) showed intense staining for SC as opposed to foci of precancerous dysplasia where, with one exception, staining was markedly reduced or absent, suggesting staining for SC could be useful in identifying foci of precancerous dysplasia in UC. In the absence of severe chronic inflammation, as in UC, the number of IgA-containing plasma cells was closely related to

SC staining of neoplastic mucosa suggesting that SC may be important in the mechanism by which IgA lymphocytes home to the lamina propria of the colon. (Author abstract) (13 Refs)

21. NUMERICAL AND STRUCTURAL CHROMOSOME ABERRATIONS IN CULTURED LYMPHOCYTES AND CUTANEOUS FIBROBLASTS OF PATIENTS WITH MULTIPLE ADENOMAS OF THE COLORECTUM.

Gardner EJ, Rogers SW, Woodward S
Dept. Biology, Utah State Univ., Logan, UT, 84322
Cancer; 49(7):1413-1419 1982

Excessive random loss and gain of single chromosomes at the diploid and tetraploid levels, and numerous chromosomal aberrations, have been observed in lymphocytes and fibroblasts, cultured from Gardner syndrome and familial polyposis coli patients and children at risk for multiple adenomas. This increase in numerical and structural aberrations seems to represent a general instability of chromosomes in the lymphocyte and fibroblast nuclei of patients with multiple adenomas in the colorectum. A consistent heteromorphism of chromosome No. 2 homologues tentatively identified as a deletion was observed in all 17 patients with multiple adenomas in the colorectum, and two younger people of 13 and 6 yr of age who are at risk for Gardner syndrome but do not have colorectal polyps. The chromosome No. 2 aberration was not observed in two symptomatic patients with occasional discrete colorectal adenomas. Eighteen controls who did not have Gardner syndrome nor familial polyposis coli did not show the structural aberration in chromosome No. 2 nor chromosome instability. (Author abstract) (21 Refs)

22. COMPARISON OF BENZO(A)PYRENE METABOLISM IN BRONCHUS, ESOPHAGUS, COLON, AND DUODENUM FROM THE SAME INDIVIDUAL.

Autrup H, Grafstrom RC, Brugh M, Lechner JF, Haugen A, Trump BF, Harris CC
LHC, NCI, Building 37/2C13, Bethesda, MD, 20205
Cancer Res; 42(3):934-938 1982

The metabolism of benzo(a)pyrene has been investigated in cultured normal human bronchus, colon, duodenum, and esophagus obtained from the same patient. The highest total metabolism was found in bronchus and duodenum, while the highest mean binding level was observed in the bronchus followed, in order, by the esophagus, duodenum, and transverse colon. A 30-fold interindividual variation in the binding level was found in each of the four organs studied, and a positive correlation between the binding levels in bronchus, colon, and duodenum was found. In human bronchus, a positive correlation was found between level of binding of benzo(a)pyrene to DNA and the amount of both benzo(a)pyrene 7,8-diol and the combined group of 3-hydroxybenzo(a)pyrene, benzo(a)pyrene 9,10-diol, and water-soluble metabolites. A significantly higher relative amount of benzo(a)pyrene tetrols and benzo(a)pyrene 9,10-diol was found by human bronchus compared to the gastrointestinal tissues, while a higher level of benzo(a)pyrene was formed by the latter. The relative distribution of benzo(a)pyrene-DNA adducts was similar in all four organs, the major DNA adduct being formed by trans-addition of anti-7,8-dihydroxy-9,10-epoxide-7,8,9, 10-tetrahydrobenzo(a)pyrene to the 2-amino group at guanine. These results indicate that the metabolism of benzo(a)pyrene by at least four different organs is qualitatively similar but that quantitative differences exist. (Author abstract) (46 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

23. SITE, EMERGENCY, AND DURATION OF SYMPTOMS IN THE PROGNOSIS OF COLORECTAL CANCER.

Pescatori M, Maria G, Beltrani B, Mattana C
Istituto di Clinica Chirurgica Universita Cattolica, Rome, Italy
Dis Colon Rectum; 25(1):33-40 1982

Four prognostic factors, ie, site of the tumors, mode of presentation, duration of symptoms, and pathologic staging, were correlated to the results of surgical treatment, ie, curative resectability, postoperative complications and mortality, and 5-yr survival, in 161 patients operated upon for colorectal cancer. Only 31 (19%) of the growths were right-sided; 71 patients (44%) had symptoms less than 6 mo. Fifty-four of them had a localized cancer; a radical procedure was performed in 114 (71%), and postoperative complications occurred in 42 cases (26%). The overall crude 5-yr survival was 38% (53 of the 140 followed-up patients). The length of the clinical history did not correlate with the pathologic staging, which greatly influenced curability and survival. A statistically significant poorer prognosis was observed in patients with left-sided tumors, with an emergency presentation and with a duration of symptoms shorter than 6 mo. A better prognosis can be achieved by means of a presymptomatic diagnosis. (Author abstract) (28 Refs)

24. PROGNOSTIC SIGNIFICANCE OF SURGICAL PERFORATION OF THE RECTUM DURING ABDOMINOPERINEAL RESECTION FOR RECTAL CARCINOMA.

Ranbarger KR, Johnston WD, Chang JC
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Am J Surg; 143(2):186-188 1982

Two hundred fifty patients were followed up after resection for carcinoma of the rectum. Sixty-four (25.6%) had a surgical perforation in the resected rectum. Perforation did not affect the long-term outcome in patients with Dukes' A or D tumors, but in patients with Dukes' B and C cancers the surgical defect was associated with an increased incidence of recurrent tumor (57 versus 34%) and a decreased 5 yr survival rate (31 versus 46%). The local recurrence rate was significantly higher in patients with Dukes' B rectal cancer who had an iatrogenic perforation (25.9%) than in those without a perforation (8.1%). This increased local recurrence rate was as high as the local recurrence rate in patients with Dukes' C cancers (23%) with or without a perforation. Patients with Dukes' B or C cancers who had incomplete resection had survival patterns similar to those in patients with Dukes' D cancers. Failure to remove all gross tumor and failure to avoid rectal perforation during abdominoperineal resection increases the risk of recurrence and decreases the chance of long-term survival. (Author abstract) (4 Refs)

25. TRANSANAL RESECTION OF BENIGN AND MALIGNANT TUMORS OF THE RECTUM BY A PULL-THROUGH FLAP. REPORT OF 267 CASES.

Faivre J, Chaume JC
Hopital Bagatelle, F 33400 Talence, France
Ann Gastroenterol Hepatol; 18(1):79-83 1982

Transanal electroresection (TAER) was used to treat 267 patients with benign (104) or malignant (163: 140 adenocarcinoma, 21 invasive degenerative villous, and 2 rare) rectal tumors. No operative mortality was reported. Postoperative complications included hemorrhage (17 cases), secondary rectal stenosis (7), incontinence (25), and urine retention (4). Six to 7 yr after the TAER, 2 recurrences were observed among the 70 patients (34 men, 36 women; 35-85 yr old) who underwent surgery for benign rectal tumors located in the lower (26 cases), middle (25), or upper (11) thirds of the rectum or higher (8) with mean diameters of 37.5-45 cm. Results are described for the first 61 patients (41 men, 20 women; mean age, 68.5) who underwent TAER for primary rectal adenocarcinomas. Adenocarcinoma diameters ranged from 19 to 49 cm and involved the submucosa (10 cases) and the first (19) or second (18) muscle layers or were perirectal (13). After a minimal follow-up of 3 yr, 37/51 adenocarcinoma patients treated by TAER were alive with no apparent recurrences, 5/51 had died from cancer, and 9/51 had died from miscellaneous diseases. The value of TAER for the treatment of rectal neoplasms is discussed. (no Refs) (In FRE)

26. EFFECT OF TINIDAZOLE PROPHYLAXIS ON THE NORMAL MICROFLORA IN PATIENTS UNDERGOING COLORECTAL SURGERY.

Kager L, Ljungdahl I, Malmborg AS, Nord CE
Dept. Surgery, Huddinge Univ. Hosp., S-141 86 Huddinge, Sweden
Scand J Infect Dis; (Suppl26):84-91 1981

Tinidazole was given during colorectal surgery and every 12 hr for 2 days postop eratively to 20 patients, including 7 with colonic and 3 with rectal cancer. Serum drug levels during surgery peaked after 30 min-3 hr; a secondary peak in serum concentration was noted in 16 patients. Fecal excretion of tinidazole was demonstrated in 7/18 patients. Enterococci and streptococci proliferated, but anaerobic bacteria declined significantly during the prophylaxis period. The patterns for colorectal microflora reversed after treatment ended. Six patients developed postoperative Escherichia coli infections. (34 Refs)

27. WHOLE GUT IRRIGATION WITH SALINE, TINIDAZOLE AND COLISTIN BEFORE COLORECTAL OPERATIONS.

Raahave D, Fris-Moller A, Jakobsen BH, Knudsen J, Bulow S
Dept. Gastroenterological Surgery, Bispebjerg Hosp., Anemonevej 24, 2970 Horsholm, Denmark
Scand J Infect Dis; (Suppl26):79-83 1981

One the day before elective colorectal surgery for cancer, 27 patients underwent whole gut irrigation with an electrolyte soln (up to 15 liters; 14 patients) or in addition 0.5 ml of a soln containing tinidazole and colistin (13 patients). The antimicrobial agents caused a significant reduction in anaerobic bacteria in the colon, but aerobic bacterial counts were not affected. The bacterial densities on the abdominal and perineal wounds were the same in both groups, but the total wound inoculum was much lower in the tinidazole-colistin group. Postoperative infections developed in 4/27 patients, all in the control group. (26 Refs)

28. SYSTEMIC PROPHYLAXIS IN COLORECTAL SURGERY: A COMPARISON BETWEEN TINIDAZOLE AND DOXYCYCLINE.

Hojer H, Brote L, Nystrom PO, Wetterfors J
Kirurgiska kliniken, Regionsjukhuset, S-581 85 Linkoping, Sweden
Scand J Infect Dis; (Suppl26):75-78 1981

Forty-three patients undergoing elective colorectal surgery (30 for colorectal cancer) were randomized to receive parenteral treatment with tinidazole (22/43) or doxycycline (21/43). The agents were equally and highly effective the prevention of deep anaerobic postoperative sepsis. (21 Refs)

29. SPHINCTER-PRESERVING OPERATIONS IN CASES OF ULCERATIVE COLITIS.

Funovics J, Kovats E, Rauhs R
I. Chirurgische Universitatsklinik Wien, Alserstrasse 4, A-1090 Wien, Austria
Langenbecks Arch Chir; 356(1):61-64 1982

Fifteen patients with ulcerative colitis were treated by sphincter-preserving ileorectostomy. One patient later required rectal extirpation. One required separation of the anastomosis. Full continence was maintained in 12/13 patients; 1/13 patient was incontinent for gas. Limitation of rectal excision to cases involving rectal hemorrhage or carcinoma is urged. (11 Refs) (In GER)

30. PRIMARY CLOSURE AND CONTINUOUS IRRIGATION OF THE PERINEAL WOUND AFTER PROCTECTOMY.

Waits JO, Dozois RR, Kelly KA
Mayo Graduate Sch. Medicine, Rochester, MN
Mayo Clin Proc; 57(3):185-188 1982

Frequency and degree of achieved primary healing (PH) were determined and factors affecting the rate of healing were assessed in a consecutive series of 152 patients who underwent rectal excision and primary closure of the perineal wound (PW) between 1975 and 1978. Patients (75 males, 77 females, 15-81 yr old, 31 operated on for rectal carcinoma, 32 for Crohn's colitis, and 89 for chronic ulcerative colitis) were followed up 2 yr or longer. The skin was prepared with povidone-iodine soap and solution. PH was defined as a dry, uninflamed wound without evidence of drainage at 30 days after removal of the drain. PH occurred within 30 days in 98/152 patients, whereas 46 patients (30.2%) healed after 30 days, and 8 patients (5.3%) failed to heal. The rate of healing varied according to the disease requiring proctectomy, sex of the patient, and site of exit of the perineal drain (PD). Patients operated on for rectal carcinoma (RC) healed primarily more often (87%) within 30 days than others (61% of those with ulcerative colitis and 50% of those with Crohn's disease). The rate of healing after 30 days was similar in the three groups. All patients with RC eventually had healing. Frequency of PH was higher in females (70%) than males (50%). The incidence of persistent perineal sinus was greater in men (28%) than in women (13%). PH was achieved more often when PD was brought through a separate incision lateral to the PW (69% of 49 patients) than when the drain exited through the wound (50% of 72 patients). The differences were largely due to the male patients with inflammatory bowel disease. Hematoma, wound abscess, and persistent perineal sinus occurred more in patients with inflammatory disease than in RC patients and the incidence was also greater in men than in women. (18 Refs)

31. ENDOSCOPIC POLYPECTOMY OF THE LARGE BOWEL: MANAGEMENT OF CANCER-BEARING POLYPS.

Kodaira S, Ono S, Purri P, Takizawa K, Kotake K, Tsuyuki A, Okuda M, Abe O

Dept. Surgery, Sch. Medicine, Keio Univ., Tokyo, Japan

Int Surg; 66(4):311-314 1981

From January 1974 to May 1979, among 2,338 endoscopic examinations of the large bowel, 184 polypectomies were performed. Forty-two cases of familial polyposis coli were excluded from this study. Of the remaining 142 cases, 21 had cancer foci: 14 were mucosally confined carcinomas, and 7 submucosally invading carcinomas. Endoscopic polypectomy was considered a radical treatment for the former and not satisfactory for the latter. Therefore macroscopic type of polyp, location of carcinoma in the polyp, and lymphatic and venous permeation were the main criteria evaluated for the strategy of treatment in cases of submucosally invading carcinoma-bearing polyps. Radical resections are necessary in cases of semipedunculated polyp with carcinoma located near the base, and in cases of pedunculated polyps with carcinoma extending to the stalk. However, as general criteria for the management of submucosally invading carcinoma-bearing polyps have not yet been established, radical resections are indicated in cases which do not fit the generally accepted criteria, in order to attempt a curative treatment. Endoscopic polypectomy therefore seems to be of great value in the early detection of colorectal cancers and their treatment. (Author abstract) (16 Refs)

32. COMBINED PRE AND POSTOPERATIVE RADIATION FOR CARCINOMA OF THE RECTUM.

Mohiuddin M, Kramer S, Marks G, Dobelbower RR

Dept. Radiation Therapy and Nuclear Medicine, Thomas Jefferson Univ. Hosp., Philadelphia, PA, 19107

Int J Radiat Oncol Biol Phys; 8(1):133-136 1982

Seventy-eight patients with invasive carcinoma of the rectum localized to the pelvis received preoperative radiation (500 rad) on the day preceding or the day of surgery. Fifty-six patients underwent an abdominal perineal resection, 10 a combined abdominal transsacral resection, and 4 a low anterior resection; eight patients were treated palliatively. Twenty-nine Stage A or B1 patients received no postoperative treatment. Of forty-one patients with Stage B2, C1, or C2 disease, 25 received the full course of postoperative radiotherapy. Sixteen patients did not receive postoperative radiation due to surgeon non-compliance with the study (9 patients), patient refusal (5), or postoperative complications (2). Follow-up ranged from 6-48 mo with a median of 18 mo. No complications from low dose preoperative radiation were observed. Mild diarrhea, which usually resolved spontaneously within 1 mo treatment, was the most common problem during the course of postoperative radiation. Five patients had a delay in healing of the surgical wound. One patient developed small bowel obstruction requiring surgery. Two patients died of postoperative complications within 1 mo of surgery. Sixty-nine patients are alive. Of 25 patients receiving both pre- and postoperative radiation, 4 patients developed distant metastatic disease. No patient in this group has failed with recurrent tumor in the pelvis. Of the 16 patients who should have but did not receive postoperative radiation, 6 patients developed recurrent cancer, 4 in the pelvis and 2 with distant metastases. The role of adjuvant radiotherapy is discussed. (14 Refs)

33. SURGICAL TREATMENT OF RECTAL CARCINOMA WITH OR WITHOUT PREOPERATIVE IRRADIATION: PRELIMINARY RESULTS OF A RANDOM TRIAL.

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Rotterdamsch Radio-Therapeutisch Instituut, Rotterdam, The Netherlands

Ned Tijdschr Geneeskd; 125(29):1148-1151 1981

Ninety patients with marginally resectable rectal carcinomas were subjected to surgery (46 patients, Group I) or to preoperative irradiation (av total dose 3,450 rads in 15 fractions, administered in 18 days, 44 patients, Group II). Radical abdominoperineal resection was performed in 30 patients in Group I and 25 in Group II, radical anterior resection in 6 and 15, incomplete resection in 3 patients in Group I, palliative resection because of hepatic metastasis in 1 patient in each group, colostomy because of inoperability or hepatic metastasis in 3 patients in Group I and in 2 in Group II. The postoperative mortality was 7/46 in Group I and 2/44 in Group II. Staging according to Duke's classification was performed after surgery in 45 patients in Group I and in 42 in Group II. Stage 0 was established in 0 and 1 patient; Stage A in 3 and 6, B in 23 and 26, and C in 19 and 9, respectively. Lymph node metastases were found in 42% of the patients in Group I and in 21% in Group II, which indicates the possibility to sterilize lymph node metastases by preopertive irradiation. Seventy-two patients survived after radical surgery: 8 of them (5 in Group I and 3 in II) developed recurrences during the follow-up period. The prognosis was more favorable in Group II than in I, but the survival rates during the first 5 yr showed no significant differences between the two groups. The survival rates were significantly higher in Stages A B than in C. (7 Refs) (In DUT)

34. DIFFERENT FRACTIONATION REGIMENS IN DISTANT GAMMA THERAPY OF RECTAL CANCER.

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Res. Roentgenoradiological Inst., Moscow, USSR

Med Radiol (Mosk); 27(1):55-58 1982

The comparative efficacy of split-course and continuous distant gamma therapy was evaluated in 96 patients (49 men, 47 women; 40-70 yr old) with rectal cancer. Only 6 patients were in Stage T2, while 90 had inoperable Stage T3-T4 tumors. Histologically, 90/96 patients had adenocarcinomas. Of 96 patients, 6 had tumors located in the ampullar region, 49 had tumors of the middle third of the rectum, and 41 had tumors of the upper third of the rectum. Group 1 (54 patients) received conventional continuous irradiations (single dose 200 rads, 5x/wk, total dose 6,000-7,000 rads). Group 2 (42 patients) received total dose of 8,000 rads in two fractions, with 3-wk interval between fractions. Immediately after completion of radiotherapy, complete tumor regression was observed in 18.5% of the patients in Group 1 and in 21.4% of the patients in Group 2. The 1-yr survivals in Groups 1 and 2 were 61.2% and 83.4%, respectively. Radiation injuries of the skin and fat (erythema, epidermitis, inflammatory infiltration) were observed in 26% of the patients in Group 1 and in 23% of the patients in Group 2. (4 Refs) (In RUS)

35. COMBINED RADICAL RADIATION THERAPY AND CHEMOTHERAPY FOR PRIMARY SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL.

Cummings BJ, Rider WD, Harwood AR, Keane TJ, Thomas GM, Erlichman TC, Fine S
Dept. Radiation Oncology, Princess Margaret Hosp., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada
Cancer Treat Rep; 66(3):489-492 1982

Radical radiation therapy (5,000 rads in 20 fractions in 4 wk) combined with iv mitomycin (10 mg/m2) and 5-fluorouracil (1,000 mg/m2/24 hr for 4 days) was used to treat 13 patients with locally advanced but operable squamous cell carcinoma of the anal canal. All patients achieved local control and retained anal continence, and none developed metastases. The patients were followed from 4 to 34 mo (median, 12). Severe acute gastrointestinal toxic effects were seen in three patients; the same patients had significant thrombocytopenia or leukopenia. Treatment with this combined program may allow conservative management of squamous cell carcinoma of the anal and should be considered as an alternative to abdominoperineal resection. (Author abstract) (11 Refs)

36. PHASE II EVALUATION OF VINDESINE FOR PATIENTS WITH ADVANCED COLORECTAL CANCER.

Saiers JH, Slavik M, McKinney DR
Hematology/Oncology Section, Veterans Admin. Medical Center, 2100 Ridgecrest Drive, SE, Albuquerque, NM, 87108
Cancer Treat Rep; 66(3):583-584 1982

A Phase II vindesine (VD) study was performed in 15 patients (14 men, 1 woman, 45-70-yr old) with advanced colon carcinomas. Histologic evidence of neoplastic disease with measurable metastatic lesions, a life expectancy greater than 1 mo, normal liver and renal functions, adequate bone marrow reserve, no edema, and adequate hydration were required. Previous chemotherapy was allowed, with a 4-wk interval after previous chemotherapy. VD was administered iv on 2 consecutive days and repeated at 7-and 10-day intervals, depending on the bone marrow and toxic effects. Patients were given 2 mg/square meter (m2) on day 1 and 1 mg/m2 on day 2. This dose schedule was predicted to achieve prolonged plasma concentrations of the drug for greater than 48 hr. An adequate trial was considered to be three courses of VD or evidence of rapidly progressing disease. Four patients received one dose of VD; three of these had obvious disease progression, and the fourth refused further therapy. One patient refused therapy after two courses. The other patients received three to eight courses. No patients responded to treatment. Three had stable disease (less than 25% regression of all measurable disease not qualifying for improvement) lasting 2-5 wk. Three patients had mild to moderate nausea and vomiting, one had significant alopecia, one had anorexia, and one had numbness and tingling of the fingers. Marrow toxicity was dose-limiting factor. It was concluded that VD given in this dose schedule had no activity in previously treated patients with metastatic adenocarcinoma of the colon. (3 Refs)

37. INTRAHEPATIC ARTERY 5-FLUOROURACIL AND MITOMYCIN-C IN PREVIOUSLY UNTREATED PATIENTS WITH HEPATIC METASTASES FROM COLORECTAL CARCINOMA.

Cowan JD, Easterbrook J, Mills GM, McCracken JD
Dept. Medicine, Brooke Army Medical Center, Ft. Sam Houston, TX, 78234
Milit Med; 147(3):220-223 1982

Fourteen patients with previously untreated metastatic colorectal cancer limited to the liver were treated with intermittent intrahepatic artery 5-fluorouracil (1,000 mg/M2, D1-D4) and Mitomycin-C (3 mg/M2, D1 and D3) every 4 to 6 wk. Toxicity was minimal, with an overall response rate of 28.6% (2 complete responses and 2 partial responses), using physical examination, liver scan, and angiography to document response. Because of the complete responses and minimal toxicities observed, more aggressive chemotherapy schedules utilizing this regimen deserve exploration. (Author abstract) (15 Refs)

38. INTERMITTENT PERCUTANEOUS INFUSION INTO THE HEPATIC ARTERY OF CYTOTOXIC DRUGS FOR HEPATIC TUMORS.

Falk RE, Greig P, Makowka L, Ambus U, Ropchan G, Larratt L, Langer B, Taylor BR, Hobbs BB, Colapinto RF, Bugala R, Gollish C, Kalman P
Univ. Toronto, 7344 Medical Sciences Bldg., Toronto, Ontario M5S 1A8, Canada
Can J Surg; 25(1):47-50 1982

Between June 1, 1976 and April 30, 1981, 157 patients were treated for inoperable cancer of the liver by intermittent percutaneous infusion of chemotherapeutic agents into the hepatic artery. The majority of these patients had metastatic colorectal cancer. The regimen of chemotherapeutic infusion evolved during the study and is described. The survival of the total group of patients is analyzed according to type of cancer, extent of disease, dosage and combination of drugs. This therapeutic modality appears to benefit patients with metastases from colorectal cancer confined to the liver. The complication rate for this procedure is relatively low. The results from this study suggest that intermittent percutaneous infusion of cytotoxic agents into the hepatic artery is worthwhile for selected patients and should be studied further in combination with other forms of therapy. (Author abstract) (14 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLO-RECTAL NEOPLASMS

39. CARCINOMA OF THE COLON AND RECTUM: THE NATURAL HISTORY REVIEWED IN 1,704 PATIENTS.

Eisenberg B, Decosse JJ, Harford F, Michalek J
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Cancer; 49(6):1131-1134 1982

For 1,704 patients with large bowel cancer compiled by the Armed Forces Central Medical Registry, selected prognostic factors were related to 5-yr or longer survival. The majority of late deaths (those occurring after 5 yr) resulted from cancer in the descending colon, sigmoid colon or rectum rather than from cancer in the right or transverse colon. For example, among all patients with cancer of the rectum, 15.4% of those with Dukes' B tumors and 10.9% of those with Dukes' C tumors died of rectal cancer be tween 5 and 10 yr after diagnosis. When late survival rates were compared, patients with right and transverse colon cancer (8 deaths/93 at risk) fared significantly better than those with left colon and rectal cancer (33 deaths/171 at risk; p = 0.01). Among patients with left-sided colon and rectal carcinoma, a further significant difference in late survival was found when stage of disease was considered: patients with Dukes' A cancers (3 deaths/47 at risk after 5 yr) fared better than those with Dukes' C cancers (21 deaths/74 at risk) (p = 0.002). For Dukes' B and C stages of disease, patients with left colon and rectal cancer fared worse than those with right and transverse colon lesions after 60 mo. Of all patients who died of large bowel cancer after 5 yr, 69% had a recurrence of cancer by 60 mo, and most late recurrences were located in the descending and sigmoid colon and in the rectum. These results show differences in survival after 5 yr with respect to both site of cancer in the colon and stage of initial disease. Our findings indicate that many left-sided large bowel cancers have a slowly progressive natural history. (Author abstract) (12 Refs)

40. EFFECT OF SEX AND REPRODUCTIVE HISTORY ON THE SURVIVAL OF PATIENTS WITH COLORECTAL CANCER.

Koch M, McPherson TA, Egedahl RD
Dept. Epidemiology, Provincial Cancer Hosp. Board, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada
J Chronic Dis; 35(1):69-72 1982

The survival rate of women with colorectal carcinoma is higher than that of men. This is true when censored survival rates are compared ($p = 0.0008$) as well as when relative survival rates are utilized to compensate for the increased life expectancy of females. Women never pregnant ($n = 56$) or women with no children ($n = 66$) showed survival rates similar to men, but significantly different to women with one or more children. The actual number of children, however, did not correlate with survival rates. (Author abstract) (21 Refs)

41. RECTAL ADENOCARCINOMA TREATED WITH INTRA-ARTERIAL 5-FLUOROURACIL. PROLONGED REMISSION.

Choy DS, Newman H, Vieta J
170 East 77 Street, New York, NY, 10021
NY State J Med; 82(3):369-372 1982

A 57-yr-old woman underwent abdominal perineal resection for an adenocarcinoma of the rectum. Serosal and regional lymph node involvement was present. Three yr later, a vaginal wall metastasis was excised. Eight yr later, an inoperable liver metastasis was found. Intravenous 5-fluorouracil failed. Intra-arterial 5-FU, however, shrank the hepatic metastasis to such an extent that it became resectable. Since this procedure was performed, the patient has survived free of gross disease for over 15 yr since the abdominal perineal resection and for over 8 yr since the liver metastasis was discovered. We attribute the long survival to aggressive chemotherapy and surgery. (Author abstract) (no Refs)

42. PATHOLOGIC FRACTURE OF MANDIBULAR CONDYLE DUE TO CARCINOMA OF THE RECTUM.

Giles DL, McDonald PJ
(c/o McDonald) Dept. Surgery, Univ. Southampton, F Level, Centre Block, Southampton, England
Oral Surg; 53(3):247-249 1982

A case of pathologic fracture of a mandibular condyle due to a primary adenocarcinoma of the rectum is presented. This is the first reported case of a secondary adenocarcinoma from the rectum to this site. Secondary metastases to the condyles are extremely rare. Only twelve have been reported in the literature. The primary tumor was from an unknown site in three cases (anaplastic adenocarcinoma); from the breast in four; and from the lung, liver, prostate, uterus, and hallux (a malignant melanoma) in the remainder. Only one of these tumors presented as a condylar fracture, and that was from a primary breast adenocarcinoma. (Author abstract) (15 Refs)

43. HEMANGIOPERICYTOMA OF THE COLON: REPORT OF A CASE AND REVIEW OF LITERATURE.

Genter B, Mir R, Strauss R, Flint G, Levin L, Lowy R, Wise L
(c/o Wise) Dept. Surgery, Long Island Jewish-Hillside Medical Center, New Hyde Park, NY, 11042
Dis Colon Rectum; 25(2):149-156 1982

A patient with a hemangiopericytoma of the colon is discussed. This is the second such case reported in the English medical literature. Soon after discovery of the tumor, the patient presented with a colonic intussusception with the tumor serving as the lead point. This was reduced by a hypaque enema, but the intussusception recurred twice more, being reduced again by hypaque enema and finally having to be reduced by colonoscopy. At surgery a left hemicolectomy with primary anastomosis was performed. The microscopic, ultrastructural, and pathologic aspects of hemangiopericytoma are discussed with special attention to lesions of the gastrointestinal tract. (Author abstract) (29 Refs)

44. MESOTHELIAL CYSTS ASSOCIATED WITH METASTASES TO OVARY FROM PRIMARY COLONIC CARCINOMA.

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(c/o Mittleman), Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Dis Colon Rectum; 25(2):139-142 1982

The three cases herein reported concern metachronous ovarian metastases from primary adenocarcinomas of the colon associated with mesothelial cysts. Although the etiology of these cysts remains obscure, the cases were of interest because the cysts did not contain tumor cells despite the intimate relationship to the tumor. Metastases were localized to the ovary and were resectable. All signs and symptoms disappeared, affording excellent palliation and an extended survival. (Author abstract) (15 Refs)

45. CYANIDE POISONING AFTER BITTER ALMOND INGESTION.

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West J Med; 136(1):65-69 1982

A 67-yr-old woman refused treatment for a resectable colonic carcinoma. Eight mo before admission, for a 2-mo period, she self-administered an injectable preparation of 'Laetrile' purchased in Mexico. Later she switched to tablets taken in an erratic manner, (probably every other day x 6 mo). A friend gave her a supply of bitter almonds, 'for medical purposes' and 'to increase her protein intake'. After the patient ingested a slurry of 4-5 bitter almonds in water, she developed symptoms of cyanide (CN) poisoning, which subsided in several hr. The patient collapsed and was hospitalized after ingestion of a slurry of 12 bitter almonds which caused severe CN poisoning, with lactic acidosis and pulmonary edema. The patient responded after stomach evacuation, use of sodium nitrite and sodium thiosulfate, and aggressive supportive care. The patient had ingested at least 70-75 mg of CN; the calculated lethal dose for her wt was 30 mg. Analysis of the patient's remaining supply of 250 mg Laetrile tablets indicated an amygdalin content of 11.5 mg (6% CN). The remaining bitter almonds showed a CN content of about 460 mg/100 g. This was a case of acute CN poisoning from bitter almonds, not chronic CN poisoning with Laetrile. (39 Refs)

46. ENZYMES OF NORMAL, PREMALIGNANT, AND MALIGNANT COLONIC CELLS.

Balis ME, Higgins PJ, Salser JS, Stemmerman GN, Magee PN, Wattenberg LW
Dept. Cell Metabolism and Cell Biochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Banbury Rep; 7:129-139 1981

The villus and crypt cells of rat small intestine contained two different forms of adenosine deaminase (AD) and adenine phosphoribosyltransferase (APRT). The APRTs of normal and neoplastic rat colonic mucosa showed similar properties. Normal colonic mucosa showed predominantly one form of AD, but colonic tumors induced by methylazoxymethanol showed two distinct forms. The ADs of human colonic mucosa and colonic cancer were also distinctive. The tumor AD was smaller than that of normal tissue and was also immunologically distinct. In rat colon, ornithine decarboxylase (ODC) activity was about the same as in liver and only 1-2% that of the small intestine. Carcinogens caused a marked increase in the ODC activity of the target tissue: acetylaminofluorene in the liver, and dimethylhydrazine (DMH) in the colon. Thymidine kinase (TK) activity of the intestine was much higher in the fetal rat than in young or mature rats. After the administration of a colonic carcinogen (DMH), the colonic TK activity increased to levels resembling the fetal TK activity. Assays using rabbit antisera demonstrated two types of TK in normal human intestine, representing the flat mucosa and the crypts. A rabbit antibody against TK from human term placenta cross-reacted against cells from a number of tumor types, including abnormal cervical cells in Papanicolaou smears and colon carcinoma cells. This antibody also reacted with skin fibroblasts from patients with familial colonic polyposis. The specificity of the TK antibody for a variety of tumor types was greatly reduced by preabsorbing the rabbit antiserum with normal human colon extracts. (11 Refs)

47. DIFFERENTIAL EFFECTS OF SODIUM BUTYRATE, DIMETHYL SULFOXIDE, AND RETINOIC ACID ON MEMBRANE-ASSOCIATED ANTIGEN, ENZYMES, AND GLYCOPROTEINS OF HUMAN RECTAL ADENOCARCINOMA CELLS.

Tsao D, Morita A, Bella A, Luu P, Kim YS
(c/o Kim) Gastrointestinal Res. Unit, Veterans Admin. Medical Center, 4150 Clement St., San Francisco, CA, 94121
Cancer Res; 42(3):1052-1058 1982

The effects of sodium butyrate, dimethyl sulfoxide (DMSO), and retinoic acid on the growth, morphology, carcinoembryonic antigen content, cell surface membrane-associated enzyme activities, and glycoprotein profiles of a human rectal adenocarcinoma cell line (HRT-18) in culture were compared. All three agents reversibly caused a marked increase in doubling times, a decrease in saturation densities, and a markedly reduced colony-forming efficiency in soft agar. Only butyrate caused gross morphological changes including cell enlargement, flattening, and increased membranous process formation. Carcinoembryonic antigen content was increased during culture in butyrate, while it was reduced by DMSO and unchanged by retinoic acid. The activities of membrane-associated enzymes were altered significantly in the butyrate-treated cells. For example, an increase in the activities of alkaline phosphatase (10-fold), gamma-glutamyl transpeptidase activity (3-fold) and sucrase activity (2-fold) was observed, while those of aminooligopeptidase and K-stimulated phosphatase actually showed slight decreases. DMSO- or retinoic acid-treated cells showed a marked decrease in alkaline phosphatase activity, but other enzyme activities remained unchanged. Surface protein-labeling patterns of lactoperoxidase-catalyzed iodinated HRT-18 cells showed no significant change from the control cells following treatment with DMSO or retinoic acid. The most prominent change caused by butyrate treatment was the appearance of a major glycoprotein band with an apparent mol wt of 60,000. These data indicate that the use of butyrate, DMSO, and retinoic acid may provide useful information concerning the identification of differentiation-associated markers of human rectal cancer cells. Furthermore, these agents, although having similar effects on the growth properties, have different effects on the morphology and on the biochemical properties of human rectal cancer cells. (Author abstract) (48 Refs)

48. ENZYMOLOGY OF PYRIMIDINE AND CARBOHYDRATE METABOLISM IN HUMAN COLON CARCINOMAS.

Denton JE, Lui MS, Aoki T, Sebolt J, Takeda E, Eble JN, Glover JL, Weber G
(c/o Weber) Lab. Experimental Oncology, Indiana Univ. Sch. Medicine, Indianapolis, IN, 46223
Cancer Res; 42(3):1176-1183 1982

The purpose of this study was to elucidate the biochemistry of human primary colon tumors and to relate the relevance of the enzymology of chemically induced, transplantable mouse tumors and human colon carcinoma xenografts to that of the human primary colon tumor. The enzymology of pyrimidine, carbohydrate, pentose phosphate, and galactose metabolism of 14 cases of primary colon tumors was compared with that of colon mucosa from the same patients. There was a marked alteration in the enzymology of the human colon tumor that distinguished it from that of the normal mucosa. In pyrimidine metabolism, there was an increase in the specific activities of the enzymes of both de novo biosynthesis [carbamoyl-phosphate synthetaseII, cytidine 5'-triphosphate synthetase, orotidine 5'-monophosphate decarboxylase, and aspartate carbamoyltransferase] and of those of the salvage pathway [deoxycytidine kinase, thymidine kinase, and uridine-cytidine kinase]. By contrast, the activity of the catabolic enzyme, uridine phosphorylase, decreased to 64%. There was a trend toward an increase in activities of enzymes of glycolysis and of pentose phosphate production. Galactokinase activity was increased four-fold. The most stringent linkage of enzyme activities in human colon neoplasia was observed for those increased in 100% of the examined cases. A comparison of the human primary colon tumors and of the experimental model systems revealed both similar and contrasting enzymic patterns. The well-defined enzymic alterations of the human primary colon tumors were in between those of the slow and the rapidly growing xenografts, forming a gradient towards the profound biochemical imbalance of the rapidly growing colon carcinoma xenograft. (32 Refs)

49. VARIATIONS OF GLYCOGEN LEVEL AND ALPHA-GLUCOSIDASE ACTIVITY IN HUMAN MALIGNANT EPITHELIAL CELL LINES IN CULTURE.

Paris H, Rousset M, Terrain B, Chevalier G, Zweibaum A, Murat JC
Institut de Physiologie, Universite Paul Sabatier, 31400 Toulouse, France
Int J Biochem; 14(2):141-145 1982

Variations of total protein and glycogen content and of alpha-glucosidase (AG) activities were determined during culture of five cell lines derived from human cancers: HRT-18, rectum; SW-839, kidney; MeWo, melanoma; SK-OV-3, ovary;

and RT-4, urinary bladder. In HRT-18 cells, neutral (pH 7) AG was found mainly in the exponentially growing cells, while lysosomal (pH 4.5) AG was preferentially increased during the stationary phase. The lysosomal and neutral AG profiles were similar in all the cell lines, and parallel to the glycogen accumulation curves; activity was very low during the early stages of cell culture and then it increased gradually. Since highest neutral AG activity coincides with the phase of maximal cell proliferation, it is proposed that its activity can be related to an enhanced synthesis of glycosylated products. Many glucose units would be used for such an anabolic process, and hence would not be available for accumulation as a reserve polymer. (29 Refs)

50. MODULATION OF PROTEIN PHOSPHORYLATION IN HUMAN COLON ADENOCARCINOMA CELL MEMBRANE PREPARATIONS BY EPIDERMAL GROWTH FACTOR IN VITRO.

Zenisek SC, Fernandez-Pol JA
(c/o Fernandez-Pol) Nuclear Medicine Lab., Veterans Admin Medical Center and Dept. Medicine, Saint Louis Univ., St. Louis, MO, 63125
Int J Cancer; 29(3):277-282 1982

Incubation of membranes prepared from the human colon adenocarcinoma cell line LoVo in vitro with [gamma-32P]ATP demonstrated numerous components whose phosphorylation was stimulated several fold by epidermal growth factor (EGF). One major component of Mn 170 K, which was either undetectable or very weakly phosphorylated in the absence of EGF, was primarily affected by exposure to EGF. The phosphorylation of the 170 K Mr membrane component required the presence of Mn; Mg was ineffective. Although the phosphorylation of many LoVo membrane components was significantly modified by cAMP or dibutyryl-cAMP, none of these cyclic nucleotides appeared to be involved in the phosphorylation of the 170 K membrane component in the presence or absence of EGF. The phosphorylation system of the LoVo membranes efficiently utilized [gamma-32P]GTP in both the basal and EGF-stimulated reactions. All the membrane components phosphorylated in the absence or presence of EGF, except a band comigrating with the tracking dye front, were digested by trypsin. The possible glycoprotein nature of the 170 K dalton phosphoprotein was indicated by the fact that the 170 K dalton band comigrated with a periodic acid-Schiff base-stained band. These findings suggest that one of the biochemical steps in the mechanism of action of EGF in LoVo cells is enhanced phosphorylation of several membrane proteins, especially that of a glycoprotein of Mr 170 K, by a membrane-bound cyclic nucleotide independent protein kinase. (Author abstract) (23 Refs)

51. EX VIVO PERFUSION OF HUMAN COLON WITH MONOCLONAL ANTICOLORECTAL CANCER ANTIBODIES.

Sears HF, Herlyn D, Herlyn M, Steplewski Z, Grotzinger P, Koprowski H
Fox Chase Cancer Center, Central and Shelmire Ave., Philadelphia, PA, 19111
Cancer; 49(6):1231-1235 1982

The binding of mouse hybridoma monoclonal antibodies directed against human colon carcinomas was studied using an ex vivo perfusion model of a freshly resected human colon segment containing a carcinoma. Tumor and the surrounding normal bowel is exposed to the putative tumor antigen through an intact vascular system without mechanical or enzymatic cellular alteration. An hour of perfusion was conducted on 30 specimens using five different monoclonal anticolorectal cancer (ACRC) antibodies. Three were gamma1, one gamma2A and one was IgM isotype. Control anti-influenza virus monoclonal antibodies were used to demonstrate absence of nonspecific binding. Our antibody 17-1A bound to the colon cancer in 7 of 10 trials, but bound to normal colon cells also in 4 of these trials. The IgM antibody did not bind to anything. The two gamma1 antibodies that recognize an antigen shed from the surface of the cell did not demonstrate cell binding under conditions of this study, and conditions to detect this will have to be modified. The ex vivo perfusion model as performed in this study can provide a valuable adjunct to evaluate the potential clinical utility for antibody conjugate radiolocalization or therapy of colon cancer. (Author abstract) (10 Refs)

52. LIMITATIONS OF GULLINO-TYPE CHAMBERS FOR COLLECTION OF INTERSTITIAL PROTEINS FROM HUMAN TUMOUR XENOGRAFTS: A HISTOLOGICAL AND THEORETICAL STUDY.

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Exp Pathol; 20(2):79-87 1981

GULLINO-type diffusion chambers, made entirely from polytetrafluoroethylene (PTFE) were implanted subcutaneously into athymic nude mice either alone or with tumor mince from a human colonic tumor xenograft. Those implanted with mince became incorporated into the resulting tumors. Chambers were removed at various times following implantation and histological sections prepared from surrounding tissues. A consistent histological picture was seen adjacent to all parts of the implants comprised of a foreign body giant cell reaction with fibrosis, irrespective of the presence of tumor. We argue that in the absence of any reaction, such chambers may collect specific proteins and allow estimation of total interstitial protein content, but are unsuitable for determining the effective in vivo concentration of any particular interstitial protein. It is further suggested that the presence of reactive tissue around the chambers could introduce further sources of error, adequate controls for which are essential for interpretation of data relating to interstitial proteins collected in this manner. (Author abstract) (27 Refs)

53. 'HIDDEN' CYTOTOXIC ANTIBODIES THAT REACT WITH ALLOGENEIC CULTURED FETAL AND TUMOR CELLS CONTAINED IN SOLUBLE IMMUNE COMPLEXES FROM NORMAL HUMAN SERA.

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Cancer Res; 42(3):881-887 1982

Hidden complement-dependent cytotoxins were demonstrated in normal donor sera after removing anti-immunoglobulins that normally block the ability of these immunoglobulin Gs to react with surface antigens on tumor cells. The blocking antibodies had certain properties of anti-idiotypes. Immunoglobulin G from Cohn Fraction II, after removing these anti-immunoglobulins, was cytotoxic for cultured fetal cells and for malignant melanoma, breast, lung, colon, and other tumor cells maintained either in tissue culture or by serial passage in nude mice. The cytotoxins were not adsorbed by extracts from normal lymphoid, liver, skin, or red blood cells. These results suggest that a heterogeneous group of natural antibodies reactive with antigens expressed on a variety of neoplastic and fetal cells circulate in normal donor sera as part of a soluble immune complex, together with a blocking anti-immunoglobulin. (Author abstract) (39 Refs)

54. PRESENCE OF 1,25-DIHYDROXYVITAMIN D3 RECEPTORS IN ESTABLISHED HUMAN CANCER CELL LINES IN CULTURE.

Frampton RJ, Suva LJ, Eisman JA, Findlay DM, Moore GE, Moseley JM, Martin TJ
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Cancer Res; 42(3):1116-1119 1982

Receptors for 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] have been described in several human breast cancer cell lines and more recently in human melanoma. The presence of 1,25-(OH)2D3 receptor (1,25-DR) in two cultured breast cancer cell lines was associated with receptors for calcitonin, another hormone thought to have effects on calcium handling. Therefore, it seemed important to examine a range of established human cancer cell lines for the presence of receptors for 1,25-(OH)2D3 and calcitonin. Thirty-three cancer cell lines were examined. 1,25-DR was found to be present in 23 lines, while calcitonin receptors were not detected in any of them. the 1,25-DR from several cell lines sedimented at about 3.5S in sucrose density gradients, had the appropriate specificity for vitamin D metabolites, had Kds of 0.8 x 2.2 x 10(-11) M, and had receptor concentrations of 12 to 99 fmol/mg protein. Ten malignant melanoma and 9 colonic carcinoma lines constituted the largest groups of carcinoma cell lines, and 7 and 8, respectively, of these were 1,25-DR positive. The high frequency of 1,25-DR positivity in the cultured colonic carcinoma cells is quite different from the low frequency of 1,25-DR in primary colonic carcinomas. It was also interesting that both of two cell lines derived from patients who had had both bone metastases and malignant hypercalcemia were 1,25-DR positive. These various cell lines may provide useful models for the examination of 1,25-(OH)2D3 action in vitro. (Author abstract) (31 Refs)

55. RESIDENTS' CORNER: THE EFFECT OF 'TISSUE-TYPE' SPECIFIC IMMUNOTHERAPY ON COLON C ANCER RECURRENCE IN A MINIMAL RESIDUAL DISEASE MODEL.

Harte PJ, Steele G, Rayner AA, Corson JM, Munroe AE, King VP, Wilson RE
Dept. Surgery, Brigham and Women's Hosp., Boston, MA
Curr Surg; 39(1):21-23 1982

Wistar/Furth rats (6-8 wk old) were inoculated with 1,2-dimethylhydrazine (DMH: 20 mg/kg, sc weekly for 16 wk) and resulting colon tumors were resected. After resection, rats were immunized with 10(6) irradiated (10,000 rad) cells from either a DMH-induced syngeneic colon sarcoma (DMH-W15) or a DMH-induced syngeneic colon adenocarcinoma; metachronous primary and recurrent tumors were resected and histologically proved. Rats receiving no immunization had local or regional recurrence within 22 wk (12/16). Those immunized with DMH-W15 cells responded similarly (15/20), but of those receiving DMH-W163 only 8/22 exhibited local or regional recurrence. In control and DMH-W15-immunized rats, recurrence was evident in about half the Dukes'/Kirklin Stage A lesions and in most stage B lesions. In contrast DMH-W163-immunized rats exhibited recurrence in 1/4 Stage A lesions, 1/3 Stage B1 lesions, and 6/15 Stage B2 lesions. The model described here is suitable for study of not only immunotherapy but also adjuvant therapy because (1) each tumor is an individual carcinogen-induced primary tumor, (2) residual disease is first reduced by resection, leaving small numbers of tumor cells in the system, and (3) the colon cancer model is analogous to cancer of the colon in humans. (3 Refs)

56. DIFFERENT SUSCEPTIBILITIES OF CULTURED MOUSE CELL LINES TO MOUSE INTERFERON.

Tsuruo T, Iida H, Tsukagoshi S, Oku T, Kishida T
Center Chemotherapy Center, Kami-Ikebukuro 1-37-1, Toshima-ku, Tokyo 170, Japan
Gann; 73(1):42-47 1982

Cultured mouse cells were treated with 3.3 to approx 10,000 units of mouse interferon for 3 days and further cultivated in fresh medium for 2 days (recovery incubation). The IC50 (concentration of drug required for 50% inhibition) of interferon was not changed much after the recovery incubation. The most susceptible cell line to interferon was B16 melanoma; the IC50 was 10.5 units per ml of medium on day 3 after the start of treatment. P388 leukemic cells, Lewis lung carcinoma cells, and colon adenocarcinoma 38 cells were moderately susceptible to interferon and the IC50s of these cell lines were 200, 80, and 180 units per ml medium, respectively, on day 3. The cells least susceptible to interferon were those of colon adenocarcinoma 26; IC50 was greater than 10,000 units per ml. In the recovery incubation, the growth of B16 melanoma cells, P388 leukemic cells, Lewis lung carcinoma cells and colon adenocarcinoma 38 cells was considerably inhibited when these cells were treated with more than 100 to approx 1,000 units of interferon per ml medium. The rate of multiplication was usually more than 1 for these cell lines, except for Lewis lung carcinoma cells where the rate of multiplication was less than 1. This indicates that interferon is not cytocidal towards B16 melanoma cells, P388 leukemic cells, or colon adenocarcinoma 38 cells, but mouse interferon is cytocidal towards Lewis lung carcinoma cells when the cells were treated with a relatively high concentration of interferon and then cultured in the medium without interferon. (Author abstract) (23 Refs)

57. INHIBITION OF MITOSIS AND ANTICANCER ACTIVITY AGAINST EXPERIMENTAL NEOPLASMS BY ETHYL 5-AMINO-1,2-DIHYDRO-3-[(N METHYLANILINO)METHYL]PYRIDO[3,4,-B] PYRAZIN-7-YLCARBAMATE (NSC 181928).

Wheeler GP, Bowdon BJ, Werline JA, Adamson DJ, Temple CG
Dept. Biochemistry, Southern Res. Inst., Birmingham, AL, 35255
Cancer Res; 42(3):791-798 1982

Ethyl 5-amino-1,2-dihydro-3-[(N methylanilino)methyl]pyrido[3, 4-b]pyrazin-7-ylcarbamate (NSC 181928) is reported to be active against several experimental neoplasms. The experimental data obtained in the present study indicate that it causes the accumulation of cells at mitosis with both cultured cells and ascites cancer cells in vivo. This effect was observed with L1210, P388, colon cancer 26, colon cancer 38, and HEp 2 cells in culture and with L1210 cells and P388 cells in mice. The agent was also active in vitro and in vivo against a line of leukemia P388 cells that are resistant to vincristine. (Author abstract) (27 Refs)

58. CLONING AND SCREENING OF SEQUENCES EXPRESSED IN A MOUSE COLON TUMOR.

Augenlicht LH, Kobrin D
Sloan-Kettering Inst. Cancer Res., New York, NY, 10021
Cancer Res; 42(3):1088-1093 1982

Polyadenylic acid-containing cytoplasmic RNA was isolated from a dimethylhydrazine-induced mouse transplantable colon carcinoma. Double-stranded complementary DNA synthesized using these molecules was inserted into the HindIII site of pBR322 using HindIII linkers, and the recombinant molecules were cloned in Escherichia coli. Clones were screened with labeled complementary DNA synthesized from the polyadenylic acid-containing cytoplasmic RNA of the tumor or normal mouse colon, liver, or kidney. Of 378 clones screened with the normal colon and tumor probes, 7 showed major increases in abundance in the tumor tissue as compared to normal, and 1 showed a major decrease. Twenty-five other sequences were found which showed smaller increases and 22 showed smaller decreases. Of 373 clones screened with tumor, colon, liver, and kidney probes, 79% exhibited little evidence of tissue specificity in expression. The data for those sequences which do show tissue-specific regulation of expression suggest that the tumor continues to express sequences characteristic of the colon but also shows a loss, or decrease, in other gene products, most of which (19 of 25) are characteristic of the colon. Finally, nine of 10 sequences which increase from low abundance in the normal colon to high abundance in the tumor are found at a moderate to high level in the liver and kidney. On the other hand, 23 of 36 sequences which show more modest increases in the tumor as compared to normal are scarce or absent in the liver and kidney. (Author abstract) (28 Refs)

59. THE INFLUENCE OF ANDROGENS, ANTI-ANDROGENS, AND CASTRATION ON CELL PROLIFERATION IN THE JEJUNAL AND COLONIC CRYPT EPITHELIA, AND IN DIMETHYLHYDRAZINE-INDUCED ADENOCARCINOMA OF RAT COLON.

Tutton PJ, Barkla DH
Dept. Anatomy, Monash Univ., Clayton, 3168, Australia
Virchows Arch [Cell Pathol]; 38(3):351-355 1982

Androgenic hormones have previously been shown to promote cell proliferation in the small intestine of rat and androgen receptors have been demonstrated in carcinomata of the large intestine of rat. In this study the influence of testosterone and of castration on epithelial cell proliferation in the small intestine, the large intestine and in dimethylhydrazine-induced colonic tumors is compared. Cell proliferation in the small intestine and in colonic tumors was accelerated by testosterone treatment, and cell proliferation in colonic tumors, but not in the small intestine, was retarded following castration. Cell proliferation in colonic tumors was also inhibited by the anti-androgenic drug, Flutamide. Testosterone and castration each failed to influence cell proliferation in the colonic crypt epithelium of both normal and carcinogen-treated animals. (Author abstract) (22 Refs)

60. EFFECT OF AGING ON THE DEVELOPMENT OF 1,2-DIMETHYLHYDRAZINE-INDUCED INTESTINAL TUMORS IN MICE.

Turusov VS, Lanko NS, Parfenov IuD
Lab. Carcinogenic Agents, All-Union Cancer Res. Center, Moscow, USSR
Biull Eksp Biol Med; 91(12):705-707 1981

Relationship between carcinogenesis and aging was studied in young (2 mo old), mature (8 mo old), and old (12 mo old) female CBA mice. Animals received sc injections of 1,2-dimethylhydrazine (DMH: 8 mg/kg, 1x/wk). Animals were followed up for 26-35 wk after the initiation of DMH administration, and the incidence of tumors of the large intestine was determined. An overall incidence of tumors in young, mature, and old mice was 13.1%, 61.0%, and 69.1%, respectively. The frequency of infiltrating tumors was 6%, 30.5%, nad 54.3%, respectively. Analysis of time-effect curves showed that the median latent period of tumor development in young mice was approx 1.8x greater than that in old mice and 1.4x greater than that in mature mice. The differences in the chemical carcinogenesis were explained by elevated activity of beta-glucuronidase in the large intestine of old mice. (7 Refs) (In RUS)

61. MORPHOGENESIS OF COLONIC CARCINOMA. ULTRASTRUCTURAL STUDIES OF AZOXYMETHANE-INDUCED EARLY LESIONS IN COLON EPITHELIUM OF FISCHER 344 RATS.

Shamsuddin AM
Dept. Pathology, Univ. Maryland Sch. Medicine, 10 S Pine St., Baltimore, MD, 21201
Arch Pathol Lab Med; 106(3):140-144 1982

Marked dilation and distortion of the crypts have been observed in the colonic epithelium of Fischer-344 rats after four to six weekly doses of azoxymethane (8 mg/kg). These changes precede malignant transformation in this model and, therefore, may be considered premalignant. Ultrastructural morphologic aspects of these crypts can arbitrarily be divided into three stages: an early stage of increased mucus secretion and 'exhausted' appearance of mucous cells; an intermediate stage of severe crypt dilation, with extreme thinning of crypt epithelium and neutrophilic emigration to the mucous pool of the crypt lumen; and a late stage characterized by repopulation of the crypts, with epithelial cells showing an increased nuclear-cytoplasmic ratio and bizarre nuclei and nucleoli. The surface epithelium between the crypts shows increased cell loss and alterations of cell membrane. Similar structure of crypts has been described in the mucosa remote from carcinoma in rats and humans, and in various precancerous changes in humans (ie, ulcerative colitis and Crohn's disease). Therefore, I propose that these lesions are significant in human colon carcinogenesis as well. (Author abstract) (14 Refs)

62. DISTRIBUTION AND METABOLISM OF NITRATE AND NITRITE IN RATS.

Balish E, Witter JP, Gatley SJ, Lipkin M, Reddy BS, Tannenbaum SR, Van Soest PJ, Magee PN
Dept. Surgery, Univ. Wisconsin Medical Sch., Madison, WI, 53706
Banbury Rep; 7:305-319 1981

Tissue distributions of nitrite (NO2) and nitrate (NO3) were studied in germfree (GF) and conventional (CV) Sprague-Dawley rats of both sexes in several feeding experiments. In some experiments, the supplementary NO2 or NO3 (1,000 ppm) in drinking water or given by gavage, was labeled with 13N. Bacteria were apparently responsible for the reduction of NO3 to NO2, because NO2 was not detected in the tissues of NO3-fed GF rats. Both ions were detected in the gastrointestinal (GI) tracts of GF rats fed water supplemented with either ion. The ions were less readily detected in the GI tracts of CV rats fed the same amounts of the ions. The 13N-labeling studies showed that the ions were distributed throughout the GI tracts of CV rats. The GI flora probably metabolized the ingested ions to compounds which could not be identified as NO2 or NO3. Whether these metabolites were harmless or harmful could not be determined by the methods used. The 13N data also showed that NO3 was secreted into the GI tract at many sites (saliva, bile, pancreatic and cecal secretions, etc), often from areas harboring a complex microbial flora. This NO3 secretion was enhanced at sites of trauma, tissue damage, or infection. These data showed the important role of the normal GI microflora in the distribution and metabolism of ingested NO3. The composition of the flora could dictate the types of NO3 metabolites formed. Urinary NO3 excretion was greater in the GF rats than in CV rats fed the same amount of NO3. The reasons for this difference were not clear. (30 Refs)

63. METABOLISM OF NITRATE.

Tannenbaum SR, Green L, Balish E, Fine DH, Van Soest PJ, Bruce ER, Goldman P, Magee PN

Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139

Banbury Rep; 7:331-341 1981

Metabolism studies of nitrate in man and rodents are reviewed. Since 15NO3-was found in the feces of the germfree rat and [15N]urea in the urine of the conventional rat, a major portion of the nitrate that does not appear in the urine must enter the colon. In the germfree rat, the nitrate remained unmetabolized and was recovered in the feces. In the conventional rat, the nitrate was reduced to NH4, converted to urea, and excreted in urine. Excess synthesis of nitrate was observed in men fed a low-nitrate diet. In man, an oral dose of nitrate was cleared effectively from the body within 36-48 hr. (9 Refs)

64. THE METABOLISM OF XENOBIOTICS BY THE INTESTINAL FLORA.

Goldman P

Div. Clinical Pharmacology, Harvard Medical Sch., Beth Israel Hosp., Boston, MA, 02215

Banbury Rep; 7:25-39 1981

In general, the metabolism of xenobiotics involves oxidation and conjugation in the liver, with reducing and deconjugating reactions mediated by the intestinal flora. Several major metabolic reactions have been identified as carried out by the intestinal flora of rodents, but major species differences present a serious obstacle to the use of animal data to clarify the role of the intestinal flora in human colon cancer. The correlation between colon cancer and protein intake is supported by the low reported incidence of colon cancer in vegetarians; but the spouses of colon cancer patients are not at an increased risk of the disease. A susceptibility factor (familial polyposis, ulcerative colitis, etc) may be required before an effect of diet can be discerned. There is experimental evidence that the intestinal flora is essentially fixed for life by contacts during the neonatal period. This suggests that dietary alterations in later life may have little effect on the bacterial composition of an individual's intestinal flora. The differences between the compositions of the fecal flora of residents of countries with different colon cancer incidence rates can be explained in many ways, but they are at least compatible with the concept of a 'national flora' determined by a 'national diet'. It is suggested that studies on possible differences in the metabolism of xenobiotics by persons at different risks of colon cancer might give significant results if the tests involved assays of fecal mutagens rather than the microbial compositions of the intestinal flora. (50 Refs)

65. MICROBIOLOGICAL CONSIDERATIONS IN INTERPRETATION OF DATA OBTAINED WITH EXPERIMENTAL ANIMALS.

Wilkins TD

Dept. Anaerobic Microbiology, Virginia Polytechnic Inst. and State Univ., Blacksburg, VA, 24061

Banbury Rep; 7:3-9 1981

The intestinal flora of rodents differs greatly from that of humans. The rodent forestomach is lined with lactobacilli, which may interact with any drug given po. Metabolically active yeasts line the secreting portion of the stomach. Large numbers of fecal bacteria may also be present, despite efforts to prevent coprophagy. The upper small intestine harbors an unusual filamentous bacterium which is poorly understood. These bacteria become attached to the host cell membranes. The first segment of the filament is modified into a specialized attachment cell that actually inserts into the host cell membrane to form intracellular bodies which are released and begin to multiply after they attach to new host cells. The terminal ileum harbors a large population of microorganisms, not closely associated with the mucosa, which metabolize oxidized compounds. Laboratory rats and mice have a small cecum because a laboratory diet provides enough nutrients whereas the cecum of wild rodents is large and harbors microorganisms that ferment complex polysaccharides of plant origin. The cecal and colonic flora of rodents consist largely of large fusiform organisms (mainly clostridia), which are not found in the human colon. Most of these species have not yet been described or named. Major dietary changes have little influence on the intestinal flora of humans, whereas dietary manipulation or starvation can cause drastic changes in the intestinal flora of rats and mice. Investigators studying dietary effects on colonic carcinogenesis in rodents should bear these differences in mind. (16 Refs)

66. FACTORS THAT AFFECT INTESTINAL BACTERIAL ACTIVITY: IMPLICATIONS FOR COLON CARCINOGENESIS.

Goldin BR, Lombardi P, Mayhew J, Gorbach SL, Tannenbaum SR, Wilkins TD, Reddy BS, Goldman P, Hill DH, Montesano R, Magee PN, Strobel HW

Dept. Medicine, Infectious Disease Services, Tufts-New England Medical Center, Boston, MA, 02111

Banbury Rep; 7:41-57 1981

Several experiments in male Fischer rats showed significant dietary effect on fecal beta-glucuronidase (B-Gase), nitroreductase (NRase), and azoreductase (AzRase) activities. Diets containing high levels of beef protein or beef fat were associated with a significant increase in these enzymes. The metabolic conversion of 2-nitronaphthalene (2-NN) or 2-naphthylamine-beta-D-glucuronide to 2-naphthylamine (an index of NRase activity) was significantly higher in beef-fed rats than in grain-fed controls. Dietary supplementation with Lactobacillus acidophilus, tetracycline, or erythromycin reduced fecal enzyme activities in the meat-fed rats to those in controls. The mutagenicity of 2-NN in a NRase-negative Salmonella strain was enhanced in the presence of liver microsomes only by a fecal extract containing NRase activity. Significant dietary effects on fecal enzyme activity were also observed in American adults (20-35 yr old). Lacto-vegetarians and strict vegetarians showed lower fecal B-Gase, NRase, AzRase, and 7-alpha-dehydroxylase activities than omnivores. No major differences were noted between the two vegetarian groups. Dietary supplementation with Lactobacillus caused decreases in fecal B-Gase, NRase, and AzRase activities in omnivores. The enzyme activities returned to baseline values after the supplementation was stopped. The high-animal protein and high-animal fat diets, which are associated with an increased risk of colorectal cancer, caused an increase in bacterial enzymes capable of generating carcinogens in the colon in the rats. The similar association between dietary habits and fecal enzyme activities in humans may provide a partial explanation for the strong positive correlation between daily beef and fat consumption and the incidence of colorectal cancer. (11 Refs)

67. FAT, FIBER, AND OTHER MODIFIERS OF INTESTINAL CARCINOGENESIS: A STRATEGY FOR PREVENTION.

Nigro ND, Van Soest PJ, Kingston DG, Bruce WR, Tannenbaum SR, Hill MJ
Dept. Surgery, Sch. Medicine, Wayne State Univ., Detroit, MI, 48201
Banbury Rep; 7:83-93 1981

Published reports on the effects of diet on intestinal carcinogenesis in rats (a process requiring a carcinogen) suggest that the influence of dietary fiber is much smaller than the influence of dietary fat. A high-fiber diet shows a protective effect only when the dietary fat level is low. The effect of a high-fat diet may be mediated through the presence of large amounts of steroids in the large intestine, interacting with the bacterial flora. Epidemiologic data on colorectal cancer in populations having different dietary habits tend to support the results of animal experiments. Further studies are needed to define the relative proportions of dietary fat and fiber for the optimal prevention of colorectal cancer. If only the levels of dietary fat and fiber are changed, it is clear that the changes must be substantial; one report suggests that a 50% reduction in fat and the consumption of bran would be required to reduce the incidence of colorectal cancer in a high-incidence population. Such drastic changes are unlikely to be accepted by the general population or even persons at high risk. It is suggested that a diet containing bran, a less stringently reduced amount of fat, and vegetables inducing benzopyrene hydroxylase in the large intestine (including cabbage, cauliflower, broccoli, and brussels sprouts) may be more acceptable, at least by persons at high risk of colorectal cancer. (28 Refs)

68. DISCUSSION: COLONIC ACTIVATION OF CARCINOGENS.

Wogan GN, Montesano R, Goldin BR, Reddy BS, Magee PN, Archer MC, Goldman P, Balish E, Newmark H, Venitt S, Wattenberg LW, Strobel HW
Massachusetts Inst. Technology, Boston, MA
Banbury Rep; 7:167-172 1981

Experiments in rat colon explants exposed to benzo(a)pyrene (BP) suggest that the colon can fully activate this series of carcinogens by the same pathways as those observed in other tissues. A tissue's sensitivity to a carcinogen is related to its capacity to activate the carcinogen (although the site of metabolic activation is not necessarily the site of tumorigenesis) and its capacity to repair DNA damage induced by that chemical. To a certain extent, the known inhibitors of carcinogenesis can be divided into two groups. Some inhibitors cause 'phase 2' detoxification (essentially, conjugation) reactions; they alter the metabolism of the mixed function oxidase (MFO) system but do not increase its activity. In the case of BP, the effect of a 'phase 2'-active inhibitor is to reduce the formation of the ultimate carcinogen. The other inhibitors of carcinogenesis, for which beta-naphthoflavone is a prototype, caused both 'phase I' and 'phase 2' reactions. MFO activity is enhanced. These agents simultaneously induce oxidative reactions (often leading to activation of the carcinogen) and enhanced detoxification reactions. The net result in most cases is protection of the host against the carcinogen. (8 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

69. THE RISK OF SECOND PRIMARIES SUBSEQUENT TO IRRADIATION FOR CERVIX CANCER.

Lee JY, Perez CA, Ettinger N, Fineberg BB
(c/o Perez) Div. Radiation Oncology, Mallinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, 4511 Forest Park, St. Louis, MO, 63108
Int J Radiat Oncol Biol Phys; 8(2):207-211 1982

The risk of developing a new primary malignancy following radiation therapy (RT), alone or combined with surgery, for invasive cancer of the uterine cervix was studied in 1,048 patients with histologically proven invasive carcinoma Stages I, II, or III, who were followed up with a median period of 4 yr. During the observation time 32 second primaries (SP) were reported. No statistically significant difference between the observed and expected number of SP was noted. Using the person yr approach, the SP incidence rate was 5.49/1,000 person-yr. Eleven SP were observed in the pelvic region: colon, rectum, endometrium, and vagina, while 20 occurred outside the pelvis. Neither the incidence of pelvic SP nor that of extra-pelvic SP was greater than expected. The time from RT to diagnosis of a SP ranged from 1 to 16 yr with a median of 8 yr for pelvic SP, and 6 yr for extra-pelvic SP. The incidence of SP increased with the stage of cervix cancer; the increase is statistically significant. Mean ages of Stage II and Stage III patients were higher than that of Stage I patients. No significant difference of a possible carcinogenic effect of RT was noted between the patients treated with RT alone (6,000-8,000 rad) and patients treated preoperatively or postoperatively (3,000-5,000 rad). SP had no impact on the survival experience of the study population in the first 5 yr after treatment; after 5 yr some deaths were observed, but patients are at higher risk of death from other causes than from SP. (15 Refs)

70. FAMILIAL JUVENILE POLYPOSIS COLI. A CLINICAL AND PATHOLOGIC OF A LARGE KINDRED.

Grotsky HW, Rickert RR, Smith WD, Newsome JF
Dept. Pediatrics, Saint Barnabas Medical Center, Old Short Hills Road, Livingston, NJ, 07039
Gastroenterology; 82(3):494-501 1982

A kindred with familial juvenile polyposis coli is described. Of 92 family members, 26 have had symptoms consistent with polyposis, and a definite diagnosis of polyposis has been made in 19. Two family members have developed colorectal carcinoma before age 40 yr. The lesion of juvenile polyposis is a characteristic nonneoplastic polyp that is distinct from the neoplastic lesion of adenomatous polyposis. Patients with this disorder develop symptoms at an earlier age than those with adenomatous polyposis. Both variants of polyposis appear to have a dominant pattern of inheritance. Patients with juvenile polyposis who present in infancy are likely to have severe symptoms and complications. Although the premalignant potential of the juvenile polyp remains in doubt, there may be an increased risk of gastrointestinal cancer in these patients and their families. (Author abstract) (16 Refs)

71. PROCANCER CLASS OF GENES AND GENERATION OF CHROMOSOME MUTATION.

Sasaki MS, Ejima Y
Radiation Biology Center, Kyoto Univ., Yoshida-konecho, Sakyo-ku, Kyoto 606, Japan
Gann Monogr Cancer Res; 27:85-94 1982

The nature of inherent mutation associated with chromosome instability and high cancer risks is discussed. Human genetic syndromes associated with chromosome instability include Fanconi's anemia (FA), ataxia telangiectasia (AT), Bloom's syndrome (BS), incontinentia pigmenti (IP), and, perhaps xeroderma pigmentosum (XP). Chromosome aberrations are primarily of the chromatid type, indicating that the chromosome mutations in these diseases arise in connection with DNA replication. FA, AT, and IP have a significantly high frequency of chromosome aberrations, while the other diseases show normal aberration rates. DNA damage left unrepaired in AT and FA cells might not be subject to repair by post-replication error-prone repair mechanisms or such a mechanism might not operate in these cells. Genetically-determined cancer proneness appears to be caused by an intrinsic sensitivity of instability to chromosome mutation; gross chromosomal change is a prime importance in mutation toward cancer. Certain types of procancer genes with dominant traits express a mutator function and promote chromosome recombination in their somatic cells. Such mutations of de novo origin occur in familial polyposis coli, Gardner's syndrome, Peutz-Jegher's syndrome, nevoid basal cell carcinoid syndrome, hereditary retinoblastoma, dominantly-inherited familial leukemia, and familial colon cancer. The nature of germinal mutations responsible for organ-specific cancer proneness is discussed. (37 Refs)

72. DEVELOPMENT OF RISK FACTOR PROFILES FOR INDIVIDUALS WITH INCREASED SUSCEPTIBILITY TO CANCER OF THE LARGE INTESTINE.

Lipkin M, Nordlicht N, Nigro ND, Wogan GN, Montesano R, Venitt S, Bruce WR, Archer MC, Wilkins TD
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Banbury Rep; 7:97-118 1981

Several populations at high risk of colorectal cancer (CRC) have been registered at Memorial Hospital, including asymptomatic persons and spouses: hereditary polyposis syndromes; site-specific CRC without polyposis; familial multiple cancers inducing CRC; and CRC patients with a second primary malignancy and a family history of CRC, cancer other than CRC, or no cancer. The registry also includes data on families having 41 cancer-free members over at least two generations. In familial CRC, the age at CRC onset differs significantly from the age at CRC onset in the general population. An attempt is being made to identify persons at high risk of CRC who are destined to develop CRC. The phenotypic characteristics collected into the 'risk profile' for patients with familial polyposis include the percentage of 3H-thymidine-labeled epithelial cells in the upper third of the colonic crypts in random biopsy specimens of flat colonic mucosa; the carcinoembryonic antigen content of colonic lavage specimens; mixed lymphocyte reactivity to allogeneic stimuli; the distribution of normal and abnormal actin concentrations in cultured cutaneous fibroblasts; and fecal concentrations of undegraded cholesterol and 7-alpha-dehydroxylase. A systematic analysis of the effects of stress on these parameters has also been started. Other risk factor profiles for other CRC risk groups are being formulated. (39 Refs)

73. BILE SALTS AND OTHER CONSTITUENTS OF THE COLON AS TUMOR PROMOTERS.

Reddy BS, Tannenbaum SR, Montesano R, Correa P, Haenszel W, Wattenberg LW
Div. Nutrition, American Health Foundation, Naylor Dana Inst. for Disease Prevention, Valhalla, NY, 10595
Banbury Rep; 7:345-363 1981

The mechanisms by which dietary components increase the risk of developing colon cancer are reviewed and etiologic factors in large-bowel carcinogenesis are discussed. Dietary fat and fiber affect fecal bile acid excretion, which may then affect carcinogenesis. Cholesterol and its metabolites are mutagenic and have colon-tumor-promoting activity. Fecal mutagens and comutagens in high- and low-risk populations for colon cancer were studied. (63 Refs)

74. BILE ACIDS IN COLORECTAL CARCINOGENESIS.

Hill MJ, Montesano R, Bruce WR, Correa P, Lipkin M, Goldman P, Tannenbaum SR, Reddy BS
Bacterial Metabolism Res. Lab., Central Public Health Lab., London NW9 5DX, England
Banbury Rep; 7:365-380 1981

A mechanism for the adenoma-carcinoma sequence in the large bowel is proposed and discussed with respect to various mutagens that have been described in fecal extracts and to bile acid metabolites. One genetic factor and at least three environmental factors are involved in the postulated mechanism. Persons who are adenoma-prone will develop colorectal adenomas only when exposed to a factor whose concentration depends on environmental conditions. Exposure to a further factor results in an increase in the size of the adenomas, and exposure to a third factor causes dysplastic changes to occur and progress, eventually leading to malignancy. (29 Refs)

75. BILE ACIDS AND CARCINOMA OF THE LARGE BOWEL.

Raedsch R
Innere Medizin IV, Medizinische Universitatsklinik, Bergheimer Strasse 58, 6900 Heidelberg, W. Germany
Inn Med; 9(1):8-15 1982

Possible correlations between high-fat diets, increased concentration of bile acids in the intestines, and the development of cancer of the colon are discussed. The following aspects of these correlations are considered: metabolism of bile acids, animal models for a relationship between bile acids and colon cancer, bile acids and intestinal bacteria, carcinogenic, cocarcinogenic, and procarcinogenic activities of bile acids, clinical significance of bile acids, and relationship between bile acids and dietary fiber. (74 Refs) (In GER)

76. FECAL MUTAGENS IN TWO JAPANESE POPULATIONS WITH DIFFERENT COLON CANCER RISKS.

Mower HF, Ichinotsubo D, Wang LW, Mandel M, Stemmermann G, Nomura A, Heilbrun L, Kamiyama S, Shimada A
Dept. Biochemistry and Biophysics, John A. Burns Sch. Medicine, Univ. Hawaii at Manoa, Honolulu, HI, 96822
Cancer Res; 42(3):1164-1169 1982

Human feces from 223 Japanese in Hawaii at high risk for colon cancer and feces from 166 Japanese of northern rural Japan at low risk for colon cancer were shown to contain mutagenic activity under five different test conditions. The first assay, using the Ames TA98 and TA100 Salmonella test, detected ether-soluble mutagens in the presence and absence of rat liver microsomes. Of these, the TA98 direct-acting mutagens are present more frequently in the feces of the high-risk population than the low-risk population at a high level of statistical significance (p less than 0.01). TA98 mutagens activated by rat liver microsomes also occur significantly more frequently in the feces of the Japanese from Hawaii (p less than 0.05). Mutagens detected by TA100 in the presence and absence of rat liver microsomes are not commonly found in either Japanese population. The second bacterial test system used to detect fecal mutagens uses Escherichia coli rec-. This system detects water-soluble fecal mutagens which are also present more frequently in the high-risk population than in the low-risk population (p less than 0.05). (Author abstract) (27 Refs)

77. FECAL MUTAGENS AND COLORECTAL POLYPS: PRELIMINARY REPORT OF AN AUTOPSY STUDY.

Correa P, Paschal J, Pizzolato P, Pelon W, Lesley DE, Stemmerman GN, Venitt S, Tannenbaum SR, Wilkins TD, Stich HF, Nigro ND, Romsdahl MM, Reddy BS, Wogan GN, Lipkin M, Wattenberg LW, Hill MJ
Dept. Pathology and Microbiology, Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Banbury Rep; 7:119-127 1981

Examination of the colons of 81 autopsied adults (greater than 50 yr old), who had died of trauma and had no known histories of recent illness, hospitalization, or antibiotic use, disclosed adenomatous polyps in 28/81 colons. No correlation was found between the presence of mutagens in colonic contents and the presence or absence of colonic polyps (7/21 and 22/53 specimens, respectively). Several possible reasons for these negative results are discussed. The study of possible correlations between mutagens and adenomatous polyps in autopsy material involves many difficulties which have not yet been resolved. (4 Refs)

78. MUTAGENS IN EXTRACTS OF GASTROINTESTINAL MUCOSA.

Stemmermann GN, Mower H, Rice S, Ichinotsubo D, Tomiyasu L, Hayashi T, Nomura A, Mandel M
Pathology Dept., Kuakini Medical Center, Honolulu, HI, 96817
Banbury Rep; 7:175-183 1981

Mucosal specimens from 60 resected stomachs (31 from stomach cancer patients) and 25 colons (11 from colon cancer patients) were assayed for the presence of mutagenic compounds in Salmonella typhimurium TA98 and TA100. The specimens for assay were not grossly involved with cancer. Nitrosated TA98 mutagens were identified in 32/60 stomach specimens, mostly from the antrum. Both sex and age seemed to play a role in determining whether the antral tissues contained mutagens. The TA98 mutagens derived from the antral mucosa were generally nitrosated derivatives of diazepam, hydroxyzine, and cimetidine (which had been used in anesthesia), which does not mean that these agents are carcinogenic in the stomach or any other organ. However, their presence in the stomach serves as a model for the in vivo generation of nitrosated mutagenic compounds. The metabolic process can occur in the absence of dietary nitrite, provided that the gastric epithelium is exposed to any one of a wide variety of amide precursors. These observations support the epidemiologic findings of an inverse correlation between stomach cancer and the intake of foods containing substances (eg, ascorbic acid and vitamin E) blocking the nitrosation process. The intestinal specimens yielded a wide variety of TA98 and TA100 mutagens, which were not characterized chemically. Some of these mutagens seemed to favor specific sites in the colon. (6 Refs)

79. PROPERTIES OF A MUTAGEN ISOLATED FROM FECES.

Bruce WR, Varghese AJ, Land PC, Krepinsky JJ, Montesano R, Wilkins TD, Van Soest PJ, Goldin BR, Reddy BS, Kingstn DG, Tannenbaum ST, Balis E, Watson JD, Mower HF
Ontario Cancer Inst., Toronto, Ontario, M4X 1K9, Canada
Banbury Rep; 7:227-238 1981

A mutagen, with strong activity on Salmonella strain TA100 without metabolic activation, was detectable (greater than 200 revertants/g) in freeze-dried feces from 4/12 healthy subjects and 4/7 patients previously operated upon for rectal cancer who were not on medication at time of study. High mutagen levels (greater than 800 revertants/g) were detected in one normal subject and one cancer patient. Mutagenicity was strong correlated with UV absorption of the substance. The UV spectrum of the mutagen resembled that of a polyene antibiotic (filipin) but its nuclear magnetic resonance spectrum did not. The available data indicate at least two hydroxyl groups but no carboxyl or benzoyl groups in the molecule. (8 Refs)

80. ISOLATION OF A MUTAGEN PRODUCED IN THE HUMAN COLON BY BACTERIAL ACTION.

Wilkins TD, Lederman M, Van Tassell RL, Wattenberg LW, Wilkins TD, Bruce WR, Goldin BR
Dept. Anaerobic Microbiology, Virginia Polytechnic Inst. and State Univ., Blacksburg, VA, 24061
Banbury Rep; 7:205-214 1981

The feces of about 30% of North Americans contain mutagenic activity in the Ames assay, and greater than 90% of this mutagenicity is due to one substance. The isolation and purification of this substance are described. Evidence indicating its production by colonic bacteria is presented. Dietary supplementation with ascorbic acid or vitamin E (3 wk each) did not affect the fecal concentration of the mutagen in three donors. Two of these donors were a married couple who ate almost every meal together, but the wife consistently excreted much more mutagen than her husband. The daily variation in mutagen excretion was completely random. The mutagen was stable under strictly anaerobic conditions and strongly fluorescent under long-wave UV light. It was extremely sensitive to oxidation, decomposing (in a manner similar to catalytic lipid peroxidation) to a substance which was neither mutagenic nor fluorescent. The mutagen acted directly on Salmonella strains TA98 and TA100 in both its crude and purified forms. The presence of microsomal enzymes reduced its mutagenicity. Since the substance was not mutagenic for the parent strain of TA98 (TA1538), it may act by causing base-pair substitutions. This substance is not the only mutagenic compound present in human feces, but it is the most active substance in the Ames test. (10 Refs)

81. POSSIBLE APPLICATIONS OF MUTAGENESIS TESTING IN CANCER EPIDEMIOLOGY.

Haenszel W, Magee PN, Tannenbaum SR, Correa P, Hill MJ, Reddy BS, Stemmermann GN, Bruce WR, Lipkin M, Nigro ND, Venitt S, Goldin BR, Hirayama T, Archer MC, Balis ME, Keefer LK, Goldman P, Balish E, Strobel HW, Eisenbrand G
Biometry-Epidemiology Program, Univ. Illinois, Sch. Public Health, Chicago, IL, 60616
Banbury Rep; 7:431-446 1981

Epidemiological applications of mutagenesis studies for stomach and large bowel cancer are reviewed. A cohort study of stomach cancer in a high-risk population in Colombia has been proposed; positive tests for mutagenicity in gastric juice samples were found only when nitrites were present. High-risk

North American populations are suitable for bowel cancer studies. Linkage of pathology, fecal chemistry, and mutagenesis data will improve screening for large-bowel cancer and help to elucidate the pathways leading to large-bowel cancer. (20 Refs)

82. CANCER INCIDENCE AND MORTALITY IN THE UNITED STATES, 1973-77.

Young JL, Percy CL, Asire AJ, Berg JW, Cusano MM, Gloeckler LA, Horm JW, Lourie WI, Pollack ES, Shambaugh EM

(c/o Berg) Dept. Pathology, Univ. Colorado Medical Sch., Denver, CO, 80262

Natl Cancer Inst Monogr; 57:1-187 1981

Data on cancer incidence and mortality in the United States between 1973 and 1977 are presented. Data are classified according to sex, race, age, and residence of the patients, anatomic site, and histologic type of cancer. For all areas, excluding Puerto Rico, the av annual age-adjusted incidence rates for all malignant neoplasms and for carcinoma in situ were 331.5 and 26.7 per 100,000, respectively. The most common primary sites of cancer were colon/rectum, breast, and lung, with age-adjusted incidence rates of 48.5%, 46.7%, and 46.7%, respectively. The three sites accounted for 42.7% of all malignant cancers. Seventy-eight percent of in situ lesions occurred in the female genital system. Av annual mortality due to malignant neoplasms for the total United States was 166.5. Of all cancer deaths, lung cancers accounted for 21.7%, colorectal 13.6%, and breast 9.2%. Considerable variation was noted in both incidence and mortality from cancer among various racial and ethnic groups. Generally males had higher cancer rates than females. Striking differences occured among the race-sex groups and geographic areas with respect to incidence of cancer by sites. An incidence-to-mortality ratio of 1.97 was obtained. Data is classified according to 304 specific anatomic sites. Distribution of the 8,968 non-Hodgkin's lymphomas is described in terms of anatomic site (24% were extra-nodal) and race. Of all malignant cancers, 51% were diagnosed in patients aged 65 yr and older. The median age for diagnosis of patients with malignant lesions was 65.4 yr compared with 37.1 yr for in situ lesions. Of all neoplasms, 34.7% were classified adenocarcinomas, 12.4% as squamous cell carcinomas, and 9.4% as duct adenocarcinomas. A comparison with previous data is presented. (14 Refs)

83. CANCER INCIDENCE AND MORTALITY IN METROPOLITAN DETROIT, 1973-77.

Swanson GM, Brennan MJ

Dept. Social Oncology, Michigan Cancer Foundation, 110 East Warren Ave., Detroit, MI, 48201

Natl Cancer Inst Monogr; 57:219-297 1981

Data on cancer incidence and mortality in metropolitan Detroit (1973-1977) are presented. Differences between data from Detroit and those obtained by the Surveillance, Epidemiology, and End Results (SEER) Program are described. Less disparity between blacks and whites occurs in incidence rates in Detroit than is seen for the total SEER population. The increase in mortality rates was greater for Detroit blacks than for blacks in all SEER areas. Cancer sites for which Detroit appears to differ considerably from the total SEER program include lung and bronchus, colon, female breast, and prostate gland. (no Refs)

84. CANCER INCIDENCE AND MORTALITY IN PUERTO RICO, 1973-77.

Martinez I

Dept. Health, Cancer Control Program, Box 9342, Santurce, Puerto Rico, 00908

Natl Cancer Inst Monogr; 57:947-977 1981

Data on cancer incidence and mortality in Puerto Rico (1973-77) are presented by primary site and sex. Both malignant and in situ lesions are considered. Puerto Rico had a higher incidence of cancer of the mouth, hypopharynx, esophagus, stomach, and penis in comparison with findings for all Surveillance, Epidemiology, and End Results (SEER) Program areas. The incidence for all SEER areas, excluding Puerto Rico, was higher for cancers of the lip, colon, rectum, retroperitoneum, lung, bronchus, pleura, melanoma of skin, breast, corpus uteri, ovary, testis, urinary bladder, kidney, brain, endocrine glands, and lymphomas and leukemias. (no Refs)

85. CANCER MORTALITY IN BARCELONA 1960-1978.

Bosch FX, Orta J, Garcia A, Juvanet J, Camprodon A, Pumarola A

Oncology Service, Hosp. de Sant Pau, Avda S Antonio M Claret, 167, Barcelona 25, Spain

Int J Epidemiol; 11(1):46-48 1982

Cancer mortality rates specific for sex and site for the 1960-1978 period are presented. The population covered is the municipal area of Barcelona. Rates have been adjusted taking as the standard population the Spanish census of 1970. Leading sites for males are lung, stomach and large intestine. Breast, large intestine and stomach are leading causes of death for females. Secular trends follow the general picture of the western industrial countries. (Author abstract) (3 Refs)

86. IMPLICATIONS OF DIETARY FIBER BREAKDOWN IN THE HUMAN COLON.

Cummings JH, Stephen AM, Branch WJ

MRC Dunn Clinical Nutrition Centre, Old Addenbrookes Hosp., Cambridge, CB2 IQE, England

Banbury Rep; 7:71-81 1981

Metabolism of fiber in the colon and implications for human carcinogenesis are reviewed. Possible hypotheses for the mechanism of the protective effect can be obtained from examining data on the dominant effects of fiber on colorectal function. Dietary fiber is extensively degraded in the colon, leading to production of short-chain fatty acids (butyrate) which may affect colonic cell function. Fiber breakdown also stimulates microbial growth in the colon, leading to increased bulk of the colonic content, faster transit rate, and rerouting of nitrogen metabolism. Fiber fermentation in the colon diverts nitrogen metabolism from ammonia formation (ammonia is more toxic to normal cells than transformed cells) to bacterial protein synthesis. If endogenous nitrite synthesis occurs in the human colon, it may arise from the oxidation of ammonia. The optimum pH for bacterial nitrification in pure cultures and natural ecosystems is alkaline (7.0-8.5). A metabolic consequence of a high-fiber diet may be reducing the colonic pH to a level unfavorable to nitrite synthesis from ammonia, leading to a reduced formation of N-nitroso compounds. The urinary excretion of protein metabolites other than ammonia declines when wheat fiber is added to the diet, showing another change in the direction of nitrogen metabolism in the colon. Any or all these events may be important in protection from colorectal cancer. (56 Refs)

87. GASTROINTESTINAL CANCER: ENDOGENOUS FACTORS.

Bruce WR, Correa P, Lipkin M, Tannenbaum SR, Wilkins TD
Ontario Cancer Inst., Toronto, M4X 1K9, Canada
Banbury Rep 7: 468 pp., 1981.

The role of diet in cancer was examined. Sessions on gastrointestinal microbiology (microbiological considerations in experimental studies, effect of diet on human fecal flora, metabolism of xenobiotics by intestinal flora, and intestinal bacterial activity and carcinogenesis), fiber (ecology of gut fermentation in man, dietary fiber breakdown in the human colon role of fat, fiber, and other modifiers of intestinal carcinogenesis in cancer prevention), host response to carcinogens (risk factor profiles for individuals at increased risk for colon cancer, fecal mutagens and colorectal polyps, enzymes of normal, premalignant, and malignant colonic cells, role of cytochrome P-450 in colon response xenobiotics, inhibitors of gastrointestinal neoplasia, colonic activation of carcinogens), mutagens (in extracts of gastrointestinal mucosa, nitrosation in stomach mucosal tissue of humans and dogs, isolation of mutagens produced in the human colon by bacterial action, structural studies and properties of mutagens isolate d from human feces, bacterial fluctuation tests of mutagenic activity in human feces, intake, formation, and release of mutagens by man), N-nitroso compounds (endogenous formation of N-nitroso compounds, analysis of human biological specimens for nitrosamines, block nitrosamine formation using ascorbic acid and alpha-tocopherol, distribution and metabolism of nitrate and nitrite in rats, analysis of nitrate, nitrite, and nitrosamines in human feces, metabolism of nitrate), bile acids and other lipids (bile salts as tumor promoters, bile acids in colorectal carcinogenesis, and analysis of feces for benzopyrene after consumption of charcoal-broiled beef) and epidemiology and design of future studies (epidemiologic tests of hypothesis relating diet and cancer, large-scale cohort study of diet and selected digestive system cancers, and possible application of mutagenesis testing to cancer epidemiology). (716 Refs)

88. PROVEN THERAPEUTICS IN RECTAL DISEASES.

Hein KE
Romanplatz 10a, D-8000 Munchen 19, W. Germany
MMW; 124(Suppl1):S24-S25 1982

Symptoms, diagnosis, differential diagnosis, development, and current methods of treatment are described for frequently reported rectal diseases. Hemorrhoids, proctitis, and anal fissures are among the diseases considered. The importance of the proctologist in prevention of colorectal cancer is noted. (12 Refs) (In GER)

89. SOME FACTORS INFLUENCING THE ECOLOGY OF GUT FERMENTATION IN MAN.

Van Soest PJ, Hill MJ, Wattenberg LW
Div. Nutritional Sciences and Dept. Animal Science, Cornell Univ., Ithaca, NY, 14853
Banbury Rep; 7:61-69 1981

In an 80-day experiment, 24 young men were fed a low-fiber basal diet (meat, eggs, mashed potatoes, and white bread) supplemented by high-fiber bread made with coarse of fine bran, cabbage powder, or wood cellulose (max fiber level, 40 g/day). The effects of the dietary fiber on digestive function varied from one fiber type to another. Particle size, hydration capacity, and fermentability were more important than the actual chemical constitution of the fiber source. A significant negative correlation was noted between the intestinal passage rate and fiber digestion. The efficiency of metabolic conversion from fermentable fiber to fecal nitrogen was greatest with coarse bran, followed by cabbage, fine bran, and cellulose. The results suggested that metabolism by colonic microorganisms and their net systems might create a metabolic sink, in which potentially toxic substances are incorporated into the microbial cellular mass. Increasing the size of the sink could become a means of detoxification by colonic microflora, since their noncarbohydrate requirements for cellular growth must be scavenged from the intestinal environment. Nitrogenous substances bound in the microbial cells are excreted in the metabolic fecal organic matter. The role of the colonic microflora as related to the intestinal environment and health may vary according to intestinal ecology and substrate availability. The nitrogen requirement of the intestinal microflora may vary from an ammonia- and amine-producing fermentation (oversupply of nitrogen) to a nitrogen-utilizing situation (insufficient supply) in which urea, ammonia, and perhaps other hazardous substances are utilized in the microbial cell synthesis. (13 Refs)

90. AFTERWARD.

Bruce WR, Correa P
Toronto Branch, Ludwig Inst. Cancer Res., Toronto M4Y 1M4, Canada
Banbury Rep; 7:447-449 1981

Epidemiologists generally agree that gastrointestinal cancer is an environmental disease and that the most important factor in the environment is diet. There is no proof that a carcinogen in the diet is relevant to human stomach or colon cancer. To what degree a mutagen is likely to be carcinogenic is unknown. The possibility of dietary intervention for cancer is discussed. Analytical epidemiological studies are necessary to place the importance of dietary or chemical factors in perspective. (no Refs)

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Diagnosis, Treatment

SERIES CT07 No. 82/08
AUGUST, 1982

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. SCREENING TESTS FOR COLON CANCER - A NEW COMPARISON BETWEEN HAEMOCCULT AND HEMOFEC: REVIEW OF 9 YEARS OF CLINICAL EXPERIENCE WITH HAEMOCCULT.

Gnauck R
Deutsche Klinik fur Diagnostik, Aukammallee, D-6200 Wiesbaden, W. Germany
Z Gastroenterol; 20(2):84-92 1982

Screening tests Hemoccult (HO) and HemoFEC (HF) for colon cancer, marketed by two different pharmaceutical companies were compared. Patients removed stool samples on three consecutive occasions, while following certain dietary rules and mailed them in. The HO test produced positive results in 149 and the HF in 129 of 3,200 patients tested. Of the 149 patients, 22 had cancer and 26 large polyps. Of the 129 patients, 20 had cancer and 25 had adenomas. Some patients with pathologies were missed by both methods, 19 had large polyps and 2 had cancer. The HO test was used routinely since 1972 and of 25,700 patients tested 873 gave positive results. Exami-

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nations were performed on the 600/873 patients, colorectal cancer was diagnosed in the 124 and large polyps in the 196. Retrospective review of charts of all patients with colorectal cancer and polyps showed that 19/143 patients with cancer had negative HO test or 13%, while 136/332 patients with polyps had negative HO test or 41%. Any kind of new tests for wide screening should be thoroughly tested and proven to be better before they are recommended as such. (21 Refs) (In GER)

2. DOUBLE CONTRAST ENEMA AND COLONOSCOPY IN POLYP DETECTION.

Fork FT

Dept. Diagnostic Radiology, Malmo General Hosp., S-214 01 Malmo, Sweden

Gut; 22(11):971-977 1981

The diagnostic accuracy of double contrast enema was assessed by colonoscopy of 250 consecutive patients with polypoid lesions that were observed at double contrast enema. The enema method detected 90% of all existing polypoid lesions, and gave false positive results in less than 3.5%. Colonoscopy revealed 91% of the lesions. Double contrast enema is suitable as a screening procedure and, when used in combination with colonoscopy, only very few polyps will escape detection. The large number of neoplastic polyps detected in this retrospective series emphasizes the necessity for a careful radiographic technique combined with colonoscopy to disclose and treat these potentially malignant lesions of the colon. (Author abstract) (46 Refs)

3. GUIDELINES FOR USE OF THE FLEXIBLE FIBEROPTIC SIGMOIDOSCOPE IN THE MANAGEMENT OF THE SURGICAL PATIENT.

Marks G, Gathright JB, Boggs HW, Ray JE, Castro AF, Salvati E

Thomas Jefferson Medical Coll., 111 South 11th St., Suite 8254, Philadelphia, PA, 19107

Dis Colon Rectum; 25(3):187-190 1982

Based on data from many clinical studies and programs, guidelines are presented for application of the flexible fiberoptic sigmoidoscope in the management of the surgical patient. The flexible fiberoptic sigmoidoscope has proved to be an instrument of extraordinary capability in detecting colorectal neoplasms with yields being two or three times greater than those of the rigid sigmoidoscope in the symptom-resolution, polyp and cancer surveillance patient categories. In addition, the practical advantages of the narrow diameter, flexibility, and length of the fiberoptic sigmoidoscope are readily appreciated when the surgeon finds that he can satisfactorily examine patients with rectal or sigmoid strictures, marked angulations, or contracted lumens in whom a rigid scope would be unsuitable. Data from the authors' comparative study of more than 3,000 patients have permitted the development of not only guidelines for the application of the flexible fiberoptic sigmoidoscope but an appreciation of the modified role of the rigid sigmoidoscope and the proper relationship between the flexible fiberoptic sigmoidoscope and the flexible fiberoptic colonoscope. A most important consideration is based on data regarding the site distribution of 400 benign premalignant neoplasms detected in the comparative study. The even distribution of these lesions throughout the terminal 50 cm of colorectum underscores the need to examine as much of the colorectum as possible. (Author abstract) (12 Refs)

4. COLON OPACIFICATION BY ORAL WATER-SOLUBLE CONTRAST MEDIUM ADMINISTRATION THE NIGHT PRIOR TO CT EXAMINATION.

Cranston PE

Radiology Dept., Univ. Mississippi Medical Center, 2500 North State St., Jackson, MS, 39216

J Comput Assist Tomogr; 6(2):413-415 1982

The technique for satisfactory opacification of the colon for computed tomography of the abdomen utilizing 1 ounce of Gastrografin orally on the night prior to scanning is presented. Two clinical cases are presented to show effectiveness of this method. The use of this technique will reduce cost, time, and effort as well as patient discomfort. (Author abstract) (7 Refs)

5. HISTOLOGICAL EVALUATION OF COLORECTAL BIOPSIES.

Balazs M, Csermely A, Vadasz G

Korbonctani Osztaly, Fov. Janos Korhaz, Budapest, Hungary

Orv Hetil; 123(7):401-404 1982

The histological evaluation of 2,351 colorectal biopsy specimens is described. Tumors were diagnosed in 1,291/2,351 cases: they included 646 adenomas, 108 pseudopolyps, 528 invasive carcinomas, and 9 rare tumors (lipomatosis of Bauhin's valve, lipoma leiomyosarcoma and cloacogenic carcinoma in 1 case each, malignant carcinoid and malignant lymphoma in 2 cases each). The adenomas included 453 pure adenomas, 144 mixed (adenovillous) polyps, and 49 villous adenomas. Highly differentiated adenomas were found in 205 cases, adenomas of medium degree of differentiation in 229, poorly differentiated adenomas in 103, and carcinoma in situ in 109. Incidence of carcinoma in situ was 11.7% in pure adenomas, 25% in mixed adenomas, and 40.8% in villous adenomas. Malignant transformation was not seen in pseudopolyps. It was possible to avoid overtreatment (surgery) by the histological investigation in two patients with submucous lipomas. (42 Refs) (In HUN)

6. PATTERN RECOGNITION IN HISTO-PATHOLOGY: BASIC CONSIDERATIONS.

Kayser K, Schlegel W

Pathologisches Institut, Universitat Heidelberg, Im Neuenheimer Feld 220, D 69 Heidelberg, W. Germany

Methods Inf Med; 21(1):15-22 1982

A computer-assisted system for identifying normal and neoplastic tissues by the patterns of the tissue structures (eg, diameter, distance, shape, and number of neighboring structures) is described. Graph theory and the theory of symmetries are used to develop two independent sets of parameters, which can be used for diagnostic purposes. Preliminary examination of low-magnification (40-80 diameter) fields of colonic mucosa disclosed significant differences between normal and neoplastic tissues. Polyps form glands that are twice as wide as normal mucosa or colonic adenocarcinoma. Carcinomas can be identified by the minimal distances between their glands. (23 Refs)

7. ELECTRON MICROSCOPIC STUDY OF CARCINOMA OF THE COLON.

Balazs M, Kovacs A

Dept. Pathology, Janos Hosp., Diosarok u. 1, H-1125 Budapest, Hungary

Exp Pathol; 20(4):203-214 1981

During electron microscopic studies of 24 carcinomas of the colon the authors compared the ultrastructural characteristics of tumorous epithelial cells of various degrees of differentiation. Beside the epithelial elements, the myofibroblast reaction, considered to be a local immune reaction due to invasive tumor cells, observable in the stroma of tumors was also treated in detail. It was observed that myofibroblasts develop from the fibroblasts of the matrix of colonic mucosa. (Author abstract) (25 Refs)

8. ULTRASTRUCTURAL ALTERATIONS IN THE COLONIC MUCUS LAYER DURING CARCINOGENESIS: A SCANNING ELECTRON MICROSCOPY STUDY.

Traynor OJ, Wood CB, Costa N
Dept. Surgery, Royal Postgraduate Medical Sch., London, England
Adv Exp Med Biol; 144:225-229 1982

Changes in the physical appearance of the colonic mucus layer (CML) during carcinogenesis were examined using scanning electron microscopy. The changes were studied in experimental animals during chemical carcinogenesis and also in humans with colorectal cancer and colonic polyps. The normal CML had a similar appearance in control animals and normal patients. Patients with colorectal carcinoma had advanced changes in the appearance of CML which were similar to those seen in rats with fully developed tumors. In patients with colonic polyps, changes were seen that resembled the preneoplastic appearances in experimental animals. (8 Refs)

9. CEA SERUM VALUES CONTROVERSY.

Satler JJ, Herzog B
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Am J Proctol Gastroenterol Colon Rectal Surg; 33(2):24,26,28 1982

Considering the hypothesis that the CEA concentrations in serum might be in proportion with CEA concentrations in malignant tissue of patients with proven colorectal carcinoma, thus explaining different normal as well as pathological values in sera, 23 radically operated patients were selected for the study. Both concentrations were estimated using radioimmunoassay of double antibodies and the values of every single patient compared. No correlation was established as in spite of high CEA productive tumors the levels of CEA concentrations in sera were found to be within normal as well as pathological range. Parallel to this study, CEA concentrations in sera and ascites of 37 patients were compared using the same method. While in malignant ascites the levels of CEA concentration were always high in the pathological range over 100 ng, the levels in sera were within normal limits in four out of seven patients. In ascites of 27 patients with liver cirrhosis CEA concentrations were always low to 30 ng/ml. It could be concluded that the reason for disproportion between carcinoembryonic antigen concentrations is highly productive malignant tissue and moderate, even normal values in sera still remains obscure and controversial. On the other hand it suggested that the estimation of CEA concentrations in ascitic fluid might be more useful for differentiating the malignant from nonmalignant ascites than CEA concentrations values in sera. (Author abstract) (7 Refs)

10. SERIAL CEA ASSAYS AND LIVER SCINTIGRAPHY FOR THE DETECTION OF HEPATIC METASTASES FROM COLORECTAL CARCINOMA.

Szymendera JJ, Wilczynska JE, Nowacki MP, Kaminska JA, Szawlowski AW
Inst. Oncology, P.O. Box 47, PL-00 973 Warsaw 22, Poland
Dis Colon Rectum; 25(3):191-197 1982

Of 340 patients with histologically proven colorectal carcinoma, hepatic metastases were diagnosed in 90 (26%), in 50 at the time of initial surgery (synchronously) and in 40 during the postoperative follow-up (metachronously). At the time of initial surgery, plasma carcinoembryonic antigen (CEA) levels were markedly elevated in patients with synchronous metastases and normal or only moderately elevated in those with metachronous metastases. During follow-up, CEA levels in the entire group of patients with metastases remained normal in 8% and rose in the remainder: very quickly in 85% and slowly in 15%. Hepatic metastases were diagnosed by strict scintigraphic criteria in 70% of patients and were suggested by liberal criteria in the remainder. During follow-up, hepatic metastases progressed in the scintigraphic image from those defined by liberal to those diagnosed by strict criteria. In two-thirds of the patients, liver scintigraphy proved to be superior to the CEA test in diagnosing hepatic metastases by strict criteria; in the majority of the remainder of patients, the CEA test, particularly in cases with a pattern of fast increase of CEA in plasma, suggested metastases before a definite diagnosis could be made by liver scintigraphy. In only 3% of the patients neither liver scintigraphy nor the CEA test were indicative of metastases. Thus, the two diagnostic modalities, when combined, could attain a sensitivity of 97%, when patients with persistently rising CEA levels and concomitant liver lesions defined by the liberal criteria were grouped with those for whom scintigraphy was unequivocal. (Author abstract) (34 Refs)

11. SENSITIZATION OF HUMAN LYMPHOCYTES TO CARCINOEMBRYONIC ANTIGEN (CEA): NEUTRALIZATION EXPERIMENTS WITH ANTI-CEA SERA.

Muller M, Irmscher J, Heidl G, Grossmann H, Wagner H, Kotzsch M, Zotter S
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Exp Pathol; 21(1):5-9 1982

By means of the macrophage electrophoretic mobility technique we could show lymphocytes of patients suffering from cancers of the digestive system to be sensitized to carcinoembryonic antigen (CEA). These findings conflict with the common view that CEA is not immunogenic in humans. The aim of the present study was to look as to whether conventional anti-CEA sera can neutralize the activity of a CEA preparation which is responsible for the human lymphocyte response. When 60 ng CEA were preincubated with highly diluted anti-CEA serum and the resulting immune complexes were thereafter co-precipitated by protein A-sepharose, positive lymphocyte responses could no longer be obtained. This effect was observed with three anti-CEA sera in three cancer patients (colon cancer, stomach cancer, teratocarcinoma), who's lymphocytes responded to CEA by lymphokine release. Normal serum had no neutralizing effect. The anti-CEA sera did not influence the activity of another tumor-relevant extract (teratocarcinoma-derived), to which cancer patients' lymphocytes reacted regardless of the tumor site. The lymphocytes from an esophagus carcinoma patient, though reacting to the teratocarcinoma preparation, did not respond to CEA, thus, logically, all other tests with normal serum and anti-CEA sera were negative, too. The results show that the digestive system cancer-associated lymphocyte reactivity to CEA can be abrogated by conventional anti-CEA sera, which finding indicates that there exist closely CEA-associated 'tumor-specific' antigenicities. (Author abstract) (18 Refs)

12. TUMOR ASSOCIATED PRODUCTS IN COLONIC LAVAGE FLUID.

Vellacott KD, Groom G, Balfour TW, Baldwin RW, Hardcastle JD
Dept. Surgery and Cancer Res. Campaign Lab., Univ. Nottingham, University Park, Nottingham NG7 2RD, England
Clin Oncol; 8(1):61-67 1982

Colonic lavage techniques have been used to look for tumor associated products in 132 patients. Carcinoembryonic antigen estimations on 83 showed higher levels in those with adenomatous polyps greater than 1 cm diameter, colonic cancers and inflammatory bowel disease than in those with no evidence of gastrointestinal pathology. Enzyme studies showed beta-glucosidase was elevated in similar groups. Using a modified C1q binding assay no difference in levels of immune complexes between the diagnostic groups was found. Carcinoembryonic antigen and glycolytic enzymes in feces may prove useful for the diagnosis of early colorectal tumors in asymptomatic screening studies. (Author abstract) (16 Refs)

13. THE TENNESSEE ANTIGEN TEST. AN EVALUATION IN CANCER AND NON-CANCER PATIENTS AND NORMAL SUBJECTS.

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Br J Cancer; 45(2):223-229 1982

The Tennagen test has been evaluated in 'normal' subjects, patients with cancer (predominantly colorectal) and patients with non-malignant disease. The incidence of positive values was found to be higher in patients with clinically active cancer than in those with benign conditions or normal subjects. In our hands the test fell far short of the 90% reliability previously claimed. This may be partly due to an underestimate of the upper normal limit in earlier studies. A small series of follow-up studies after resection for colorectal cancer have so far failed to reveal any advantage to be gained by Tennagen tests over existing methods, but these studies will be continued. (Author abstract) (10 Refs)

14. ANTIBODY PATTERN TO HUMAN CYTOMEGALOVIRUS IN PATIENTS WITH ADENOCARCINOMA OF THE COLON.

Avni A, Haikin H, Feuchtwanger MM, Sacks M, Naggan L, Sarov B, Sarov I
(c/o I. Sarov) Virology Unit, Faculty Health Sciences, Ben Gurion Univ. Negev, Beer Sheva, Israel
Intervirology; 16(4):244-249 1981

The role of human cytomegalovirus (CMV) was examined according to serological patterns in 37 patients with adenocarcinoma of the colon (ACC). The sera were examined for the presence of IgG antibodies by the immunoperoxidase antibody to membrane antigen (IPAMA) method and by the complement-fixation (CF) test. Antibody determinations were also performed by the IPAMA method for three other members of the herpesvirus group: Epstein-Barr virus (EBV), herpes simplex virus (HSV) and varicella-zoster virus (VZV). Comparison groups included normal subjects, ACC patients treated with chemotherapy, and patients operated on for benign diseases. No significant difference was found in the geometric mean titers (GMTs) for CMV and the other herpesvirus in the sera of nontreated ACC patients when compared with the control groups. However, a significantly elevated antibody titer to CMV was found in chemotherapy-treated ACC patients by both the IPAMA and CF methods. In this group, elevated titers were found by the IPAMA method for EBV and HSV, but not for VZV. The significance of serological studies in elucidating the role of CMV in ACC patients is discussed. (Author abstract) (30 Refs)

15. IMMUNE REACTIVITY IN COLORECTAL CARCINOMA: CLINICAL VALUE FROM A SURGICAL VIEWPOINT.

Muhrer KH, Schwemmle K, Filler D, Kahle M
Chirurgische Universitatsklinik, Klinikstrasse 29, D-6300 Giessen, W. Germany
Chirurg; 53(2):112-116 1982

Specific immune reactions to colorectal carcinoma (CRC) were studied. NaCl extracts of tumor cell-membrane proteins were made from samples of CRC, gastric cancer (GC), bronchial carcinoma (BC), and mammary carcinoma (MC). CRC types included well, moderately, and poorly differentiated adenocarcinoma. Lymphocytes preparations were made from venous blood of 36 patients with histologically confirmed CRC, 15 patients with precancerous adenoma of the colon, 19 patients with inflammation of the colon, and 54 healthy controls. Reactivity to tumor antigens was measured by inhibition of electrophoretic cell migration using sheep RBC as indicator cells. Inhibition of greater than 5% was considered positive. Positive reactions to CRC extract were obtained with lymphocytes from 31/36 CRC patients. Average inhibition was 12.0 +-7.03% for Duke's Stage A CRC, 11.18 +-5.06% for Stage B, 13.26 +-7.03% for Stage C, and 16.80 +-7.65 % for patients with extensive metastases. Negative results were obtained from 48/56 controls. Positive results were obtained from 10/15 patients with adenoma and 11/19 patients with inflammatory conditions. Of 36 CRC patients, 8 showed positive reactions to GC extracts; none showed positive reactions to BC or MC. Reactivity to allogeneic tumor extracts indicated the sensitivity was specific for the tumor type rather than for the individual. Results indicate specific sensitivity of lymphocytes from CRC patients to CRC antigens and some weak cross-reactivity to antigens from other tumor types. Reliability of the test is limited by positive sensitivity of patients with acute inflammatory conditions. (15 Refs) (In GER)

16. IMMUNOPATHOLOGY OF CANCER OF THE LEFT COLON AND RECTUM. EVALUATION OF SOME PARAMETERS RELATED TO IMMUNOLOGIC RESPONSE OF THE HOST.

Naves A, Pollastri E, Dip O, Mancuso O, Puig N, Bravo Luna M, Amerio N, Morini JC
Centro de Onsologia, Hospital N del Centenerio, Rosario, Argentina
Rev Fac Cienc Med Univ Nac Rosario; 14(2):19-22 1981

Thirty patients (both sexes, 36-76 yr old) with cancer of left colon and rectum were treated by colectomy or coloproctectomy. Sections of original tumors, sections of tumors proximal and distal, and regional lymphatic ganglions (RLG) were examined. Staging according to TNM (tumor, lymph node, metastasis) indicated that 24 of the patients had neoplastic invasion reaching adipose tissue beyond muscle tissue and that 12 of the 24 had metastases in the RLG. Indexes of malignity of the tumors (IMT) were calculated, based on tumoral invasion, cortical and paracortical hyperplasia, local immune response (mononuclear cells in the border of the tumoral invasion), and perivascular lymphocytosis. Also at the time of diagnosis, peripheral blood was removed and concentrations of E rosettes were determined. The IMT was lower in patients who had curative surgery and was negatively correlated with age and with the concentration of E rosettes. It was concluded that local and general immunity of the host should be evaluated for better understanding of the physiopathology and evolution of the neoplastic process. (5 Refs) (In SPA)

17. CULTURED HUMAN T-CELL LINES KILL AUTOLOGOUS SOLID TUMOURS.

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Immunol Lett; 3(4):237-241 1981

An investigation concerning the possibility that the cytolytic activity of autoreactive T-cells, present in various lymphocyte preparations from cancer patients, might be amplified by expansion of the relevant subpopulations in T-cell growth factor (TCGF; Interleukin 2), is presented. Lymphocytes from peripheral blood, lymph node, spleen and tumor of seven patients with various carcinomas (2 lung, 3 colon, 1 stomach) and a parotid tumor, were cultured for 15 days in conditioned media containing TCGF. Cytotoxic activity was then determined against autologous tumor (and some autologous normal) cells and allogeneic tumor targets as evaluated in a short-term 51Cr-release assay. Significant cytotoxicity was detected in at least one effector preparation from all patients. This result was obtained under conditions where, in some cases, other autologous cells (normal lung, phytohemagglutinin-transformed lymphocytes) were resistant. The cytotoxicity also generally extended to allogeneic tumor targets, but lysis of K562, a cell line sensitive to natural killing, occurred in only 3/19 effector cell preparations. The results represent the first demonstration of cytotoxicity in human cultured T-cells (CTC) directed against autologous solid human tumor cells. The data are consistent with a polyclonal expansion of CTC of tumor-bearing patients which includes the amplification of a population recognitive of antigens expressed on autologous neoplastic cells. (19 Refs)

18. CLINICAL ASPECTS OF GASTROINTESTINAL MUCUS.

Forstner G, Wesley A, Forstner J

Kinsmen Cystic Fibrosis Res. Centre, Hosp. for Sick Children, Toronto, Canada

Adv Exp Med Biol; 144:199-224 1982

Histochemical studies of gastrointestinal mucus in peptic ulcer disease, parasitic infections, cystic fibrosis, adenocarcinoma, and inflammatory bowel disease are reviewed. Evidence, particularly in the colon, suggests that mucins produced by adenocarcinoma and even transitional mucosa in the neighborhood of the tumor are abnormal. Sialomucins are increased at the expense of sulfomucins. Mucins produced by tumor cells share antigenic determinants with mucus glycoproteins from normal tissue. Antisera to the colonic mucoprotein precipitate antigens from adenocarcinoma extracts. (110 Refs)

19. ALTERATIONS IN HUMAN COLONIC MUCIN OCCURRING WITH CELLULAR DIFFERENTIATION AND MALIGNANT TRANSFORMATION.

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Proc Natl Acad Sci USA; 79(6,part1):2051-2055 1982

The binding of fluorescein isothiocyanate (FITC)-conjugated lectins to mucin in the human colon was studied by using fluorescence microscopy. In normal mucosa, lectins that preferentially bind to exposed N-acetyl-galactosamine residues (Dolichos biflorus agglutinin and soybean agglutinin) bound selectively to the goblet cell mucin of well-differentiated cells in the upper colonic crypt. By contrast, lectins that require exposed non-reducing galactose residues for binding (Ricinus communis agglutinin1 and Bauhinia purpurea agglutinin) preferentially labeled the mucin of less-differentiated goblet cells located in the lower portion of the colonic crypt. The lectin derived from Arachis hypogaea (peanut agglutinin) has a high affinity for a carbohydrate structure not normally exposed in human tissues. This lectin did not label the goblet cell mucin in the normal colon. However, the mucin was labeled in all 21 colon cancer specimens examined. Additionally, the nonmalignant epithelium immediately adjacent to colon cancer (termed 'transitional mucosa') also contained goblet cell mucin that was labeled by FITC-peanut agglutinin. Three conclusions may be drawn from the selective binding characteristics of FITC-lectins to colonic mucins. First, an alteration in the exposed, nonreducing carbohydrate residues occurs in human colonic mucin during the process of goblet cell differentiation. Second, an exposed carbohydrate structure that is not normally present in human tissues is expressed in the mucin produced by malignant colonic epithelium. Third, the presence of the cancer-associated carbohydrate structure in the mucin of transitional mucosa suggests that this tissue may be in the process of early malignant transformation. (Author abstract) (26 Refs)

20. SENSITIVITY AND SPECIFICITY OF THE FECAL OCCULT BLOOD TEST FOR COLORECTAL NEOPLASIA.

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Gastroenterology; 82(5,part1):986-991 1982

The significance of tests for occult blood in the feces (OBF) for detection of colorectal tumors (CRT) is reviewed. Chemical tests for OBF are based on chemical reactions with Hb. Such tests are simple, inexpensive, and have widespread applicability. The impregnated guaiac slide test (GST) is currently being evaluated as a screening test for CRT, both as a mail-in test for asymptomatic patients over age 50 and in combination with proctosigmoidoscopy in patients over age 40. The sensitivity and specificity of the GST are apparently affected by storage, rehydration, and dietary content. Positive reactions may fade or disappear with time. Peroxidase activity due to compounds in the diet other than human Hb may lead to false positive reactions, reducing the specificity of the GST. Comparisons of the GST with radioassay procedures have shown discrepancies between the two methods. These discrepancies are due in part to the parameters being measured. The GST is capable of detecting 0.12 mg Hb/ml. The test is not quantitative, however; sampling of feces is random, and Hb may lose some pseudoperoxidase activity as it passes through the digestive tract. Determination of the value of the GST as a screening method for CRT requires further studies. (27 Refs)

21. DETECTION OF COLORECTAL TUMORS BY THE HEMOCCULT (R) TEST.

Ollivier JP, Foll Y, Rousseau M, Pauna B, Poitier L, Laurent H, Charles JF, Magadur A
Medecine A, H.I.A. Clermont-Tonnerre, 29240 Brest Naval, France
Med Armees; 9(2):117-121 1981

Hemoccult test (HT) results were examined in 648 patients. HT had been offered to a total of 1,623 patients. Of the 42 positive patients, 6 were not examined. Rigid rectoscopy and double contrast barium enema was used to evaluate the remaining 36 patients with positive HT results. Ten coloscopies were performed, 5 of them in patients in whom radiographic and rectoscopic studies gave no explanation of positive HT results. In 15 cases, non-tumoral proctologic disorders were responsible for positive HT results. Five patients with polyps were identified, four patients with a single polyp and one with two. One patient with a polyp of the antrum was observed along with three patients with colonic diverticulosis. Neither colitis nor colorectal cancer were observed. The number of positive HT increased with patient age. The value of the HT in the prevention and diagnosis of colorectal cancer is discussed. The specificity and sensitivity of the HT is considered along with a discussion of cost factors and therapeutic factors that may interfere with test results. (27 Refs) (In FRE)

22. CHEMICAL OR IMMUNOLOGICAL EVIDENCE OF OCCULT BLOOD IN STOOL IN THE EARLY DIAGNOSIS OF COLORECTAL CARCINOMA.

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Dtsch Med Wochenschr; 107(8):307-310 1982

The values of chemical and immunological tests for occult blood (OB) in the stool are compared based on a review of literature. The value of any OB. test depends on the sensitivity and specificity of the test. Chemical OB tests produce false positive results in 5-15% of cases. Available chemical tests are not specific for human Hb. As a result, animal and plant hemoproteins in the diet may be detected in the stool. OB distribution in the stool may be quite uneven, leading to misleading results of random sampling. Tests using 51Cr or 59Fe have a sensitivity approx double that of other chemical tests and can detect losses of 10 ml or more blood/day. Colorectal polyps and carcinomas may cause blood losses as small as 1-20 ml/day. Immunological OB tests detect human Hb or peptide chains of Hb at levels of 0.075 ml or less blood/100g stool homogenate. Immunological methods are currently not economically feasible as screening methods, however. Patients to be examined should, therefore, avoid dietary hemoproteins and large amounts of ascorbic acid prior to chemical OB tests. Tests should be performed on 3-6 successive stools. All patients with positive chemical results should be tested by immunological methods. Only patients with positive immunological or radioisotopic test results should undergo endoscopic or radiological studies to determine the source of bleeding. (8 Refs) (In GER)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

23. REDUCED POSTOPERATIVE MORTALITY BUT UNCHANGED THERAPEUTIC RESULTS IN PATIENTS WITH COLORECTAL CANCER UNDER THE AGE OF 30-40 YR.

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Lakartidningen; 79(11):1001-1004 1982

The therapeutic results obtained in 1,061 patients (52% men, 48% women, median age 64 yr) with colorectal cancer during the period 1950-1979 are reported. Colon cancer was diagnosed in 62% of all patients, rectal cancer in 36%, and multiple synchronous tumors in 2%. Surgery with curative intent was performed in 69% of all patients, and palliative surgery in 31%. Chemotherapy or radiotherapy was administered to individual patients. The postoperative mortality was 6% after surgery with curative intent. The overall 5-yr survival rate for the patients treated during the period 1950-1974 was 34%, increasing rates were found in 47% of the 575 patients subjected to surgery with curative intent during the period 1950-1974 (47% at the beginning and 58% at the end of this period) after correction for the successive reduction of the postoperative mortality. The 5-yr survival rates of the patients operated on with curative intent was strongly correlated with Dukes' stages: 82% in Stage A, 44% in B and 21% in C. The increase in the percentage of the patients in Stage A from 23% to 33% had only a marginal effect on the overall prognosis. (15 Refs) (In SWE)

24. COLO-RECTAL CARCINOMA: A DECADE OF EXPERIENCE AT OHIO VALLEY MEDICAL CENTER.

Kalla AH, Mahan JH, Voss EC
Colon and Rectum Dept., Univ. Texas, Houston, TX
W Va Med J; 78(3):61-69 1982

A retrospective study of 298 patients (134 males, 164 females; 75% greater than or equal to 70 yr old) with colorectal carcinoma who were followed for 5 yr or more or until death is presented. Of the 242 patients treated surgically, 84.4% underwent primary resection. Local, regional, or distant recurrences occurred in 20% of patients; 83/99 living patients were free of disease. Patients with the highest 5-yr survival were in the fifth or sixth decades. All tumors were diagnosed by barium enema or proctosigmoidoscopy. Of 324 total lesions, 116 were located in the right colon, 99 in the left colon, 27 in the rectosigmoid, and 82 in the rectum. All lesions were adenocarcinomas; two thirds were well-differentiated and 9.2% poorly differentiated. Single lesions were found in 93.6% of patients. One third had an associated polyp. Multiple primary malignant lesions were found in 9.5% and a second primary lesion developed in 7.4%. Metastases to the liver alone occurred in 48 patients, to the lymph nodes alone in 43, and to both in 26. Late metastases were found in the liver in 16.5%, bone in 5.7%, lung in 6.6%, and brain in 4.1%. Right hemicolectomy was performed in 33.6% of resected patients, sigmoid resection in 13.6%, low anterior resection in 5.8%, and abdominoperineal resection in 6.8%. Complications in 24 patients included sepsis, and respiratory, urological, or cardiovascular problems. Anastomotic recurrence occurred in 12/162 patients who underwent curative resections. Postoperative mortality was 3.8%. Two-thirds of the asymptomatic patients and one-third of the symptomatic patients survived for 5 yr. Only 28% of those with lymph node metastases survived for 5 yr. All patients who refused treatment or had a combination treatment died within 1 yr. (30 Refs)

25. POSTOPERATIVE FOLLOW-UP STUDIES ON CANCER OF THE COLON AND RECTUM.

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Natl. Cancer Center Hosp., Tsukiji 5-chome, Chuo-ku, Tokyo, Japan
Am J Surg; 143(3):293-295 1982

We followed up 790 patients with cancer of the colon and rectum treated at our hospital since 1962. The curative resection rate in the rectum and anus was 78% but decreased as the distance of the lesion from the anus increased. In the ascending colon the rate was 59.8%. The patients undergoing curative resection had a 5-yr survival rate of 65% and a 10-yr survival rate of 45%. The closer to the anus, the poorer the prognosis. Prognosis is greatly influenced by the stage at diagnosis. Surgical results have improved annually due to progress in diagnostic and therapeutic procedures. Factors greatly influencing prognosis were the presence of lymph node metastasis, the degree of invasion of the intestinal wall and the site of the primary lesion. Lymph node metastasis was an especially important prognostic factor. In cancer of the rectum primary recurrences were most often found in local sites (66% of cases), followed by metastasis to the liver and the lung. However, in cancer of the colon metastasis to both the liver and the peritoneum was observed in 67% of the cases. On the basis of these results, methods to prevent local recurrence of cancer of the rectum as well as metastasis to the liver from cancer of the colon must be developed. When extended abdominopelvic wide dissection was performed, the incidence of local recurrence decreased. (Author abstract) (5 Refs)

26. INTEREST IN THE FOLLOW-UP OF PATIENTS AFTER ENDOSCOPIC RESECTION OF COLORECTAL POLYPS FOR CANCER PREVENTION: 123 CASES.

Aubert H, Treille C, Faure H, Fournet J, Lachet B, Rachail M
Clinique Medicale B, C.H.U. de Grenoble, F-38043 Grenoble Cedex, France
Gastroenterol Clin Biol; 6(2):183-187 1982

Of 263 patients who underwent polypectomy, 123 patients (86 men, 37 women; 50-70 yr old) treated for 182 adenomatous polyps were re-examined in follow-up studies to determine the number of patients with new polyps, the histologic type of new polyps, parameters related to recurrence, and the ideal delay in follow-up for such patients. Eighty-one new polyps were discovered in 47/123 patients. New polyps were more often found in men (36/87) than in women (11/37). The incidence of recurrence did not vary with patient age. Tumor characteristics, including histologic type, size, type of implantation, or site, showed no correlation with the incidence of recurrence. Recurrences were usually of the same histologic type as the initial polyp: 18/19 of recurrences with mild dysplasia and 17/20 of those with marked dysplasia or malignant changes. The incidence of recurrence increased with time following polypectomy. The results confirmed the necessity of follow-up after polypectomy but did not identify significant risk factors. (26 Refs) (In FRE)

27. RECTAL CARCINOMA: TREATMENT AND RESULTS.

Cardoen G, Van den Daelen L, Boeckx G, Hartono F
Dienst Heelkunde, Stedelijk Ziekenhuis, Roeselaere, Belgium
Acta Chir Belg; 81(1):41-50 1982

One hundred and fifty-one patients (84 men and 67 women) with rectal carcinoma were subjected to surgery during the period 1963-1980. Anterior resection was performed in 49 patients, pull-through operation in 35, abdominoperineal resection in 58, and other types of surgery in 9. Sphincter-preserving surgery was performed in 58.3% of all patients. The overall postoperative mortality rate was 11.9% (2.1% during the period 1976-1980 due to improved postoperative reanimation). The corrected 5-yr survival rates were 58.5% (67.7% after anterior resection, 66% after pull-through operation and 48% after abdominoperineal surgery). The corresponding crude 5-yr survival rates were 46.7% (67.7% after anterior resection, 54.2% after pull-through operation and 36.2% after abdominoperineal surgery). The corrected 10-yr survival rates were 49.7% (66% after anterior resection, 44.5% after pull-through operation and 40.6% after abdominoperineal resection). The corresponding crude 10-yr survival rates were 21.9% (38.2% after anterior resection, 16.7% after pull-through operation and 12.8% after abdominoperineal resection). (24 Refs) (In DUT)

28. MORTALITY, MORBIDITY, AND PATTERNS OF RECURRENCE AFTER ABDOMINOPERINEAL RESECTION FOR CANCER OF THE RECTUM.

Rosen L, Veidenheimer MC, Coller JA, Corman ML
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Dis Colon Rectum; 25(3):202-208 1982

Records of 230 patients who underwent abdominoperineal resection between 1963 and 1976 were reviewed. The median age of the patients was 62 yr. The mortality rate was 1.7%, and the morbidity rate was 61%. One hundred eighty patients were followed for 5 to 13 yr to identify patterns of recurrence. Ten-yr survival for Dukes' A, B, and C lesions was 83%, 57%, and 31%, respectively. Seventy-eight patients (43%) had recurrent cancer; 10% had local lesions, and 33% had distant lesions. Dukes' B lesions had a greater latency for local recurrence than Dukes' C lesions. Dukes' A lesions with distant recurrence had a greater latency than Dukes' B or C lesions. Once recurrence was established, the survival rate was not significantly different, regardless of Dukes' stage or local or distant site. Radiation therapy for established local recurrence or chemotherapy for established distant recurrence did not seem to alter survival rates. (Author abstract) (27 Refs)

29. COMBINATION CHEMOTHERAPY OF ADVANCED COLORECTAL CANCER UTILIZING 5-FLUOROURACIL, SEMUSTINE, DACARBAZINE, VINCRISTINE, AND HYDROXYUREA: A PHASE III TRIAL BY THE EASTERN COOPERATIVE ONCOLOGY GROUP (EST: 4275).

Engstrom PF, MacIntyre JM, Douglass HO, Muggia F, Mittelman A
American Oncologic Hosp., Philadelphia, PA
Cancer; 49(8):1555-1560 1982

Patients who had measurable evidence of recurrent or metastatic colorectal carcinoma following surgery and radiotherapy but no prior chemotherapy were randomized to one of five combination chemotherapy programs. Four of the treatments utilized 5 consecutive days of fluorouracil (FU) (Days 1-5 and Days 36-40) plus one oral dose of semustine (ME) (Day 1) every 10 wk: (A) FU + ME; (B) FU + ME + vincristine (VC) (Day 1 and Day 36); (C) FU + ME + dacarbazine (DC) (Days 1, 2, 36, 37); (D) FU + ME + VC + DC. The fifth treatment option (E) used a weekly treatment program of FU iv on Day 1 plus hydroxyurea (HU) PO on Day 4. The overall response rate was 13% (60/472) and the median survival time from start of therapy for all patients was 31 wk. The response rate and the median survival time for each combination was

(A) 9/103 = 9%, 26 wk; (B) 10/92 = 11%, 28 wk; (c) 15/101 = 15%, 37 wk; (D) 11/91 = 12%, 27 wk; (E) 15/85 = 18%, 38 wk. There is no statistical difference in response rate or survival duration among any of the treatment options. The therapies containing DC produced the only complete responses (3 patients on treatment C and 2 on D). Treatment D was also associated with the longest median response duration (Treatment D = 55 wk). Treatment A (FU + ME) was associated with the highest incidence of life-threatening toxicity. (Author abstract) (20 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

30. COLORECTAL LINITIS PLASTICA.

Rao TR, Hambrick E, Abcarian H, Salgia K, Recant WM
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Dis Colon Rectum; 25(3):239-244 1982

Primary linitis plastica of the colon is an uncommon tumor, with only 22 cases having been previously reported. Experience with two men and one woman between 17 and 55 yr of age, portraying a spectrum of clinical presentations ranging from rectal bleeding to large-bowel obstruction, is reviewed. Clinical and radiologic characteristics and histologic features helpful in making the diagnosis are detailed. Though the prognosis is grim, resective surgery, including oophorectomy in women, should be undertaken. Adjuvant therapy has been disappointing. (Author abstract) (15 Refs)

31. SURVIVAL WITH CARCINOMA ARISING IN MUCOSAL ULCERATIVE COLITIS.

Lavery IC, Chiulli RA, Jagelman DG, Fazio VW, Weakley FL
Dept. Colon and Rectal Surgery, Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH, 44106
Ann Surg; 195(4):508-512 1982

Adenocarcinoma of the colon is a well-recognized complication of total chronic ulcerative colitis. The incidence increases with time, and the carcinoma arising in chronic ulcerative colitis has developed a bad clinical reputation in terms of aggressive behavior. The survival statistics of patients with cancer arising in chronic ulcerative colitis are compared with statistics for a group of noncolitic patients with equivalent clinicopathologic staging treated at the same institution. When grouped by extended Duke's classification and compared with carcinoma arising without ulcerative colitis, there was no statistical difference in survival rates. The overall results are worse because of the higher percentage of patients with incurable disease at the time of operation. With improved surveillance and methods of detecting premalignant changes, the necessity for prophylactic proctocolectomy should decline. (Author abstract) (28 Refs)

32. MULTIPLE PRIMARY CARCINOMAS OF THE COLON AND ASSOCIATED EXTRACOLONIC PRIMARY MALIGNANT TUMORS.

Lee TK, Barringer M, Myers RT, Sterchi JM
Dept. Surgery, Bowman Gray Sch. Medicine, 300 S. Hawthorne Road, Winston-Salem, NC, 27103
Ann Surg; 195(4):501-507 1982

A review of 308 cases of colorectal carcinoma showed 12 cases (3.9%) of colorectal multiple primary malignant tumors and 14 cases (4.5%) of colorectal primary malignant tumors associated with extracolonic primary malignant tumor. A total of 60 tumors was involved: 14 each in the sigmoid and transverse colon; 8 in the cecum; 6 in the rectum; 1 each in the ascending and descending colon; 3 each in the bladder and prostate; 2 each in the breast, cervix, and lung; and 1 each in the skin, nasopharynx, kidney, and endometrium. Three of the four patients with multifocal cancer were found to have in situ cancer, and 12.7% of concomitant adenomas had malignant changes. Seven patients had regional lymph node metastases. Of the six patients with rectocolonic multiple tumors who had adequate follow-up data, survival in three ranged from 19.5 to 60 mo; three were alive and well 15 and 51 mo after resection. Survival of patients with primary rectocolonic and extracolonic tumors was similar. From these data and the pathologic study of the resected specimens, we recommend for any patient with cancer of the rectocolon that the entire colon be searched for multiple primary malignant tumors, that extracolonic tumors be considered second primary tumors unless proved to be metastases, and that follow-up be long and include frequent rectocolonic examinations for a second primary tumor. (Author abstract) (37 Refs)

33. THE NATURAL HISTORY OF COLORECTAL CARCINOMA IN ADOLESCENTS.

Odone V, Chang L, Caces J, George SL, Pratt CB
(c/o Pratt), St. Jude Children's Res. Hosp., P. O. Box 318, Memphis, TN, 38101
Cancer; 49(8):1716-1720 1982

The symptoms, histology, extent, and course of disease of 24 adolescents with colorectal carcinoma who were admitted to Saint Jude Children's Research Hospital between 1964 and July 1980 are presented. Twenty of the patients were referred between October 1974 and June 1980. Most patients presented with vague abdominal complaints. Twenty-one of the 24 patients had poorly differentiated mucin-producing adenocarcinoma. Extensive disease at diagnosis and unresponsiveness to medical management was reflected in the 8-mo median survival for diagnosis. Only 2 of the 24 patients survive free of disease 15 and 130 mo from diagnosis. Two other patients survive with disease at 4 and 24 mo. (Author abstract) (18 Refs)

34. COLORECTAL CARCINOMA IN PATIENTS LESS THAN 40 YEARS OF AGE.

Ohman U
Dept. Surgery, Karolinska Hosp., S-104 01 Stockholm, Sweden
Dis Colon Rectum; 25(3):209-214 1982

The mean incidence of colorectal carcinoma in persons under age 40 in Sweden is 1.74/100,000/yr. Over a 30-yr period, 1950 through 1979, 1,061 patients with colorectal carcinoma were seen, 48 of whom were under age 40 (21 to 39 yr) and in this study were compared with older patients. Carcinoma was superimposed upon ulcerative colitis in 18 patients. All patients treated for palliation died within 2 yr. Curability rate, 67%, and the proportion of Dukes' A lesions were the same as in older patients, whereas young patients had fewer B and more C lesions. Five-yr survival was 33% overall and 50% in curable cases, not different from the rates in older patients (33 and 47%). Five-yr survival was 100% in stage A, 50% in stage B, and 33% in stage C. The age factor had no impact upon survival, and colitic origin of a carcinoma did not decrease survival more than did carcinoma itself. It is concluded that colorectal carcinoma in patients under age 40 differs in no respect from the disease in older patients. (Author abstract) (22 Refs)

35. RECENT DEVELOPMENTS IN 'NONSPECIFIC' INFLAMMATORY BOWEL DISEASE. (FIRST OF TWO PARTS).

Kirsner JB, Shorter RG
Univ. Chicago Hospitals and Clinics, Box 319, 950 E. 59th St., Chicago, IL, 60637
N Engl J Med; 306(13):775-785 1982

Definition of inflammatory bowel disease (IBD), differentiation of ulcerative colitis and Crohn's colitis, complications, pathology, malignant processes in IBD, and medical and surgical treatment are reviewed. Patients with total ulcerative colitis lasting longer than several yr are at increased risk for carcinoma of the colon and rectum, which develops at an earlier age and has a tendency toward multiple lesions and a right-sided colonic distribution. Cancer of the colon and rectum complicating IBD is difficult to identify early, since the symptoms mimic those of IBD and the tumors are often small and flat. Guidelines currently used in surveillance of patients with longstanding IBD are presented. (194 Refs)

36. EXTRACORPOREAL IMMUNOADSORPTION OF PLASMA FROM A METASTATIC COLON CARCINOMA PATIENT BY PROTEIN A-CONTAINING NONVIABLE STAPHYLOCOCCUS AUREUS: CLINICAL, BIOLOGICAL, SEROLOGIC, AND HISTOLOGIC EVALUATION OF THE PATIENT'S RESPONSE.

Ray PK, Idiculla A, Mark R, Rhoads JE, Thomas H, Bassett JG, Cooper DR
Dept. Surgery and Microbiology, Medical Coll. Pennsylvania and Hosp., Philadelphia, PA, 19129
Cancer; 49(9):1800-1809 1982

A patient with a metastatic colon carcinoma was treated by immunoadsorption (IA) therapy using heat-kiled, formalin-stabilized protein A-containing Staphylococcus aureus Cowan I as the immunoadsorbent. The patient experienced both subjective and objective positive clinical response without undue morbidity. The patient's response correlated with the laboratory findings of decreased concentrations of carcinoembryonic antigen (CEA), immunoglobulin G (IgG), immune complexes (IC) and histopathologic data. The patient underwent surgery following 15 IA treatments; she lived for 18 mo post-treatment. (Author abstract) (50 Refs)

37. TOXICITY AND ANTICANCER ACTIVITY OF A NEW TRIAZINE ANTIFOLATE (NSC 127755).

Corbett TH, Leopold WR, Dykes DJ, Roberts BJ, Griswold DP, Schabel FM
Southern Res. Inst., Birmingham, AL, 35255
Cancer Res; 42(5):1707-1715 1982

A new triazine folate antagonist 3-chloro-4- *4- 2-chloro-4-[4,6-diamino-2,2-dimethyl-s triazin-1(2H)-yl]phenyl* butyl benzenesulfonyl fluoride compounded with ethanesulfonic acid (1:1) (NSC 127755), was highly active against four transplantable colon adenocarcinomas (36, 38, 10/A, 12/A) and the Dunning murine ovarian tumor M5076. Treatment schedule studies indicated that a prolonged time of exposure provided optimum antitumor activity for the compound. The combination of NSC 127755 plus 4-amino-1-[5-O-(1-oxohexadecyl)-beta-D arabinofuranosyl]-2(1H)- pyrimidinone (palmO-ara-C, NSC 135962) was found to have therapeutic synergism against grossly evident colon adenocarcinoma 36. (Author abstract) (19 Refs)

38. CARCINOEMBRYONIC ANTIGEN (CEA) EXPRESSION IN SOMATIC CELL HYBRIDS.

Sheer D, Brown RM, Bobrow M
Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England
Somatic Cell Genet; 8(1):1-13 1982

Five intraspecific somatic cell hybrids formed between a human carcinoembryonic antigen (CEA)-producing colonic tumor cell line, LS174T, and a HeLa derivative that does not produce CEA, BU25.CAPR, were investigated for expression of CEA. The viable LSB clones (16, 20, 44, 45, and 46) all contained BU25.CAPR marker chromosomes; the clones all produced substantial CEA but less per cell than LS174T. The number of chromosomes lost in the hybrids compared with parental cells ranged from 3-17. Seven hybrid clones (LSPG) were formed between LS174T and the mouse melanoma cell line, PG19, and 28 hybrid clones (LSR) were formed between LS174T and the mouse kidney adenocarcinoma cell line RAG. The hybrids retained between 4 and 21 human chromosomes, and each human chromosome was represented in at least seven hybrids. Trace amounts of CEA were found in two hybrids, suggesting either repression of CEA production by the mouse genome or production of a structurally abnormal CEA molecule. (29 Refs)

39. THE EFFECT OF WARFARIN ON SPONTANEOUSLY METASTASISING COLORECTAL CANCER IN THE RAT.

Mooney B, Serlin M, Taylor I
Dept. Surgery and Pharmacology, Univ. Liverpool, Liverpool, England
Clin Oncol; 8(1):55-59 1982

A study of the effect of warfarin on the natural history of azoxymethane-induced colorectal cancer in the rat has been carried out. Fifty rats were treated with azoxymethane in a dose of 10 mg/kg/wk for 12 wk. They were then divided into two groups. One group act as a control while the other was treated with warfarin (0.2 mg/l drinking water) for 6 wk. Insofar as was possible coprophagy was prevented. Adequate anticoagulation was achieved. The animals were allowed to survive until signs of advanced disease developed. Laparotomy and post-mortem were then carried out. The number of primary colorectal tumors in the warfarin treated group (155) was statistically significantly less than that in the control group (225). The number of lung and liver metastases were also statistically significantly reduced in the warfarin treated group (4) compared to the control group (12). This study suggests that not only does warfarin have antimetastatic properties but apparently inhibits primary tumor growth also. (Author abstract) (16 Refs)

40. INHIBITION OF METHYLAZOXYMETHANOL-INDUCED INTESTINAL TUMORS IN THE RAT BY PYRAZOLE WITH PARADOXICAL EFFECTS ON SKIN AND KIDNEY.

Notman J, Tan QH, Zedeck MS
(c/o Zedeck), Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Res; 42(5):1774-1780 1982

Methylazoxymethanol is a potent carcinogen and induces tumors predominantly of the small intestine and colon following a single injection. Previous data indicated that alcohol dehydrogenase could convert this carcinogen to a reactive alkylating agent. Rats were treated with an inhibitor of this enzyme, pyrazole, 2 hr prior to their receiving the carcinogen.

The development of intestinal and colonic tumors was prevented. The rats did, however, develop numerous tumors of the skin and kidney. Analyses of the complete autopsies are presented. The data indicate that intestinal and colonic alcohol dehydrogenase plays a role in the tumorigenic effects of methylazoxymethanol and that other non-pyrazole-sensitive enzymes exist in other organs that can also activate this carcinogen. (Author abstract) (21 Refs)

41. INDUCTION OF ORNITHINE DECARBOXYLASE IN COLON AND LIVER BY STARVATION AND REFEEDING: A COMPARISON OF EFFECTS ON TOTAL AND HOLOENZYME.

Stanley BA, Kazarinoff M

Div. Nutritional Sciences and Section Biochemistry, Molecular and Cell Biology, Div. Biological Sciences Cornell Univ., Ithaca, NY, 14853

Biochem Biophys Res Commun; 105(2):773-777 1982

Short-term starvation and refeeding induced both the total and holo-ornithine decarboxylase (ODC) levels in the colon of rats. After brief starvation alone, a significant decrease in total ODC was observed in the colon; there was no effect on colon holo-ODC. Similar effects on total ODC level were seen in the liver; neither starvation-refeeding nor starvation alone had any effect on liver holo-ODC levels. This is the first demonstration of the dietary induction of ODC in the colon. It is of interest to investigate whether this induction simply reflects a compensatory increase in general protein synthesis following starvation, or whether it represents a specific induction such as that observed during tumor promotion by chemical carcinogens. (18 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY AND CARCINOGENESIS

42. CANCER MORBIDITY AMONG WOODWORKERS IN THE U.S. AUTOMOTIVE INDUSTRY.

Swanson GM, Belle SH

Dept. Social Oncology, Michigan Cancer Foundation, 110 East Warren, Detroit, MI, 48201

JOM; 24(4):315-319 1982

In October 1979, concern was expressed about suspected excess cancer among woodworkers in several automobile manufacturing plants of the major automobile corporations located in Detroit. Cancer incidence rates for this group were compared with corresponding data for white males in the Detroit metropolitan area. Determination of standardized morbidity ratios (SMRs) showed significant increases for all types of cancer combined and for colorectal and salivary gland cancer in the study group. Further investigation is required to determine whether occupational exposure is responsible for these increases or if some other etiological mechanism is operating. (Author abstract) (38 Refs)

43. MORTALITY AND CANCER MORBIDITY AMONG WORKERS IN THE RUBBER TIRE INDUSTRY.

Delzell E, Lewis J, Monson RR

(c/o Monson) Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115

Am J Industr Med; 2(3):209-216 1981

Mortality and cancer incidence were evaluated retrospectively in 1,792 white men employed at a rubber tire plant between 1954 and 1976. The 1,792 workers had accumulated 26,839 person-yr of follow up. Among men employed for 10 yr or more, overall cancer mortality was approx 19% higher than that expected in Connecticut white males, whereas cancer incidence for all sites combined was similar in the two groups. Excesses in deaths and incident cases for cancers of the buccal cavity and pharynx, large intestine, pancreas, and kidney were observed. The workers also showed excesses in deaths from cancers of the digestive organs and peritoneum and incident cases of cancer of the bronchus and lung. No increase in occurrence of stomach or bladder cancer or of leukemia was seen. Limitations of the data are discussed in terms of interpreting the results. As the workers investigated were young (93% total person-yr less than 65 yr old), and because estimates of cancer excesses were conservative in this study, cancer mortality and morbidity should continue to be monitored in the rubber industry. (15 Refs)

44. EPIDEMIOLOGY OF CARCINOMA OF THE COLON AND RECTUM IN IRELAND: MORTALITY ANALYSIS.

Habba SF, Daly L, Doyle JS
St. Laurence's Hosp., Dublin 7, Ireland
Ir J Med Sci; 151(1):6-11 1982

Mortality patterns of cancer of the colon and rectum in Ireland are compared with those of the rest of the world and with respect to age, sex, and geographical distribution within Ireland. Mortality data from the reports on vital statistics (1950-1976) and unpublished data from the Central Statistic Office were used for calculations. International comparisons are based on World Health Organization publications. Time trends were calculated using the indirect method of standardization with 1975 age and sex specific rates chosen as standard, and a standardized mortality ratio was calculated for each year from 1950-1976 using the population figures obtained from the latest census. Geographic variation analysis was based on the combined mortality data from 1973-1975. Even after standardization, Ireland maintains its position with the highest incidence of mortality from malignant neoplasms of the intestine excluding the rectum in males and the second highest in females. The study confirms the continual rise in mortality from cancer of the colon (excluding rectum) in contrast with the trends in England and Wales; the need for early detection of these carcinomas is stressed. (7 Refs)

45. ASSESSING HUMAN EPIDEMIOLOGIC DATA ON DIET AS AN ETIOLOGIC FACTOR IN CANCER DEVELOPMENT.

Enstrom JE
Sch. Public Health, Univ. California, Los Angeles, CA
Bull NY Acad Med; 58(3):313-322 1982

Assessment of the relationship between diet and cancer is reviewed. Epidemiology of cancer among human populations consists of randomized, controlled trials based on interpretation of naturally occurring phenomena. The strongest epidemiologic data relating diet to cancer are geographic correlations between such factors as per capita fat consumption and age adjusted colon and breast cancer rates. Weaknesses exist in such correlation: large variation in colon cancer rates occurs within the United States (US), even when fat intake remains constant. Studies of Japanese who migrate from Japan to the US provide another form of epidemiologic evidence for a correlation between diet and cancer. Japanese emigrants in the US have increased rates for colon and breast cancer as compared to native Japanese; such selective use of epidemiologic data is partially contradicted by other data which indicate that the overall total cancer rate among Japanese Americans remains unchanged, with a total death rate lower than that of native Japanese. Specific populations which maintain diets different from the average American diet are discussed, using as examples Mormons and Mexican Americans. No data has demonstrated any specific relationship between diet and cancer rate. (26 Refs)

46. NUTRITION AND CANCER: MECHANISMS OF GENOTOXIC AND EPIGENETIC CARCINOGENS IN NUTRITIONAL CARCINOGENESIS.

Weisburger JH, Horn C
American Health Foundation, Valhalla, NY, 10595
Bull NY Acad Med; 58(3):296-312 1982

Mechanisms of carcinogenesis are reviewed with regard to type of chemical carcinogen - genotoxic, cocarcinogen, or promoter. Examples and mode of action are given for each. The role of epigenetic agents in nutritionally linked cancers, particularly large bowel or colon cancer, is discussed; specific dietary elements considered relevant through studies in human and animal models are the amount of dietary fat and fiber and mode of cooking. The operation of these elements is through epigenetic mechanisms, which are dose and time dependent. A reduction in dose should lead to lowering of risk, which may eventually be applied to humans through dietary adjuvant therapy. (71 Refs)

47. DIETARY FIBER AND DISEASE.

Kritchevsky D
Wistar Inst. Anatomy and Biology, Philadelphia, PA
Bull NY Acad Med; 58(3):230-241 1982

The association between dietary fiber and disease is reviewed. Classification of fiber is based on chemical components of the main chain; various fiber classes (pectins, hemicellulose, cellulose, lignin) have different physiological actions in humans. The possible association between levels of dietary fiber and colon cancer and atherosclerosis is discussed. A diet high in complex carbohydrates (high fiber diet) has resulted in reduced serum cholesterol and glucose and also reduced insulin requirements. No directly positive influence of dietary fiber on lipid metabolism and colon cancer has consistently been found. (77 Refs)

48. DIETARY FIBER.

Kay RM
Dept. Surgery, Toronto Western Hosp., Univ. Toronto, Toronto M5T 2S8, Canada
J Lipid Res; 23(2):221-242 1982

Dietary fiber is plant-derived material that is resistant to digestion by human alimentary enzymes. Fiber may be divided into two broad chemical classes: (1) non-alpha-glucan polysaccharides (cellulose, hemicelluloses, and pectins) and (2) lignins. Dietary fiber behaves within the gastrointestinal tract as a polymer matrix with variable physicochemical properties including susceptibility to bacterial fermentation, water-holding capacity, cation-exchange, and adsorptive functions. These properties determine physiological actions of fiber and are dependent on the physical and chemical composition of the fiber. Fiber undergoes compositional changes as a consequence of bacterial enzymatic action in the colon. Dietary fiber is of clinical significance in certain disorders of colonic function and in glucose and lipid metabolism. Dietary fiber increases stool bulk by acting as a vehicle for fecal water and by increasing fecal bacterial volume. Use of fiber in the treatment of constipation and uncomplicated diverticular disease is well established. By increasing stool bulk, fiber also reduces the fecal concentration of bile acids and other substances. Certain types of fiber decrease the rate of glucose absorption and attenuate postprandial rises in blood glucose and insulin. Plasma cholesterol levels are reduced by mucilaginous forms of fiber. This effect appears to be mediated in part by an increase in fecal acidic sterol excretion. (Author abstract) (266 Refs)

49. FIBRES, NUTRITION AND THE GUT.

Schrijver M, Tytgat GN

Dept. Internal Medicine, Div. Gastroenterology, Univ. Amsterdam, 1 e Helmerstraat 104, 1054 EG Amsterdam, The Netherlands

Neth J Med; 25(2):49-55 1982

The constitution of dietary fiber and its normal function and fate in the gastrointestinal tract are reviewed. Potential for carcinoma of the colon and rectum and other diseases as a result of fiber deficiency is discussed. Conducting and/or interpreting most studies is complicated by both the nonstandard nature of 'fiber' and its interactions with intestinal microflora and bile. (70 Refs)

50. CHOLECYSTECTOMY AND THE INCIDENCE OF CANCER OF THE LARGE BOWEL.

Weiss NS, Daling JR, Chow WH

Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104

Cancer; 49(8):1713-1715 1982

As part of an epidemiologic study of cancer of the large bowel in women, female residents of King and Pierce counties (Washington) who were diagnosed during 1976-77 were interviewed regarding previous gallbladder surgery. Their responses were compared with those of a random sample of women from the same population. A history of cholecystectomy was somewhat more frequent among patients with colon cancer than among controls - we estimate the colon cancer risk in women without a gallbladder to be 1.4x that of other women - but the 95% confidence limits of the relative risk included 1.0 (0.8-2.5). There was no association between cholecystectomy and rectal cancer and, among the subsites of colon cancer, the magnitude of the excess risk failed to show any consistent right-left gradient. Nonepidemiologic data suggest that cholecystectomy could increase the risk of colon cancer. However, if such an association truly exists it is not a strong one, and studies larger than those conducted to date are needed to detect this association reliably. (Author abstract) (15 Refs)

51. GARDNER'S SYNDROME: SIX GENERATIONS.

Palmer TH
431 State St., Bangor, ME, 04401
Am J Surg; 143(4):405-408 1982

A family of 68 members in six generations has been investigated, and thus far 23 of these have had colorectal polyposis, cancer or both. Many of the 23 have had a variety of soft tissue lesions, occult osteomas of the mandible, and dental abnormalities. Six of nine siblings in the proband's immediate family had diffuse colorectal polyposis and soft tissue lesions, as have 4 of their 20 children. One of three members of the most recent generation has polyposis and skin lesions. Retrospectively, 2 of the proband's 18 maternal cousins had colorectal polyposis or cancer, as did five of six siblings in her mother's generation. Four of nine siblings in the previous generation died from colon cancer, and so did their father. In the first three generations cancer was prevented in only 1 of 10 patients. Two of 13 in the later three generations thus far have died from colorectal cancer. Both coloproctectomy and colectomy with preservation of the rectum have been utilized in the patients in this study. Lifelong follow up is underway for those whose rectum has not been removed. (Author abstract) (24 Refs)

52. AUTOSOMAL DOMINANT MUCOID COLON CARCINOMA: A STUDY OF A CASE AND A KINDRED.

Budd DC, Fink DL
Dept. Surgery, St. Joseph Hosp. and Medical Center, Barnert Memorial Hosp., 707 Broadway, Paterson, NJ, 07503
Am Surg; 48(4):180-183 1982

Autosomal dominant mucoid colon cancer syndrome is reported in a black family living in the eastern United States. Presently, 17 patients in the kindred have had cancer, including 14 with colon carcinoma and others with renal, bladder, or endometrial carcinomas. One patient had mucoid colonic cancer, atypical endometrial hyperplasia, and leiomyosarcoma. The case of one of the kindred, a 28-yr-old woman who presented with fatigue and anemia, is described. Barium enema revealed a large annular constricting lesion at the hepatic flexure and a second lobulated polypoid lesion at the cecum. An extended right hemicolectomy with ileotransverse colostomy was performed. Discovery of metastases in 2/14 lymph nodes necessitated iv 5-fluorouracil chemotherapy. Vital cancer statistics were collected by questionnaire on a total of 110 individuals of the family, including 84 relatives and 26 unrelated spouses. Earlier onset of malignancy was found in generations two (52.4 yr of age) and three (34.0 yr of age). Approx 50% of individuals in generation two and 25% in generation three have thus far developed cancer. The adenocarcinomas of the colon are invariably of the mucoid type. The tumors have no special location in the colon and range from 2.5-5.6 cm in diameter. In one instance, synchronous mucoid carcinomas in the cecum and hepatic flexure were found. Metastases are almost always present. (8 Refs)

53. CORRELATES OF HOMOSEXUAL BEHAVIOR AND THE INCIDENCE OF ANAL CANCER.

Daling JR, Weiss NS, Klopfenstein LL, Cochran LE, Chow WH, Daifuku R
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
JAMA; 247(14):1988-1990 1982

To determine whether characteristics that are correlated with male homosexual behavior are associated with the incidence of cancer, the names of persons with a diagnosis of cancer in western Washington during 1974 to 1979 were linked to those in the state syphilis registry. Eight of 47 men with anal cancer were found to have had a reactive FTA test result; the expected number, based on the proportion of reactive cases among men with other sites of cancer, was only 0.40. Among men with anal cancer identified through 10 population-based cancer-reporting systems in the United States, 24.4% had never been married, compared with 7.8% of men with colon and rectal cancer. Neither of these relationships was observed for women with anal cancer. Because in men, but not in women, having had syphilis and being single are associated with the practice of anal intercourse, our data suggest that anal intercourse may be a risk factor for anal cancer. (Author abstract) (19 Refs)

54. PHENOTYPIC VARIATION IN HEREDITARY ADENOMATOSIS: UNUSUAL TUMOR SPECTRUM.

Lynch HT, Ruma TA, Albano WA, Lynch JF, Lynch PM
Dept. Preventive Medicine, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178
Dis Colon Rectum; 25(3):235-238 1982

Familial adenomatous polyposis coli is a heterogeneous disease with respect to genetics as well as its colonic polyposis and cancer phenotype. The authors report a family with variation in phenotypic expression of polyps ranging from isolated polyps to florid carpeting of the entire colonic mucosal surface. In addition to early-onset colonic cancer, a patient with isolated polyps had a seminoma and subsequently developed gastroesophageal cancer. His son, also with isolated colonic polyps, manifested a pararectal rhabdomyosarcoma. The significance of these variations can only be assessed fully through the study of cancer of all anatomic sites in many additional families. (Author abstract) (6 Refs)

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PHILIP C. HANAWALT Stanford University	*Cellular Responses to Damaged DNA*	#VK03 54 min.
CHARLES HEIDELBERGER University of Southern California	*Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells*	#VK04 54 min.
FRED RAPP Milton S. Hershey Medical Center	*The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation*	#VK05 52 min.
	Panel Discussion	#VK06 31 min.

MECHANISMS OF METASTASIS

ISAIAH FIDLER Frederick Cancer Research Center	*The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy*	#VB01 47 min.
GEORGE POSTE Smith, Kline and French Laboratories	*Phenotypic Analysis of Metastatic Cell Populations*	#VB02 42 min.
LANCE LIOTTA National Cancer Institute	*Tumor Cell Invasion of Basement Membranes and Extracellular Matrices*	#VB03 33 min.
EVERETT SUGARBAKER Miami Cancer Institute	*Some Clinical Characteristics of Metastasis in Man*	#VB04 41 min.

AUTOMATED CYTOLOGY

Part One: Principles and Techniques	#VB05 56 min.
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COLO-RECTAL CANCERS

Diagnosis, Treatment

SERIES CT07 No. 82/09

SEPTEMBER, 1982

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. CURRENT STATUS OF FECAL OCCULT BLOOD TESTING IN SCREENING FOR COLORECTAL CANCER.

Winawer SJ, Fleisher M, Baldwin M, Sherlock P
Dept. Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
CA; 32(2):100-112 1982

Early diagnosis of colorectal cancer vastly improves survival rate; fecal occult blood testing has been used in the past but was thought to be clinically unreliable. The test was recently reintroduced as the guaic paper slide test. The guaic undergoes phenolic oxidation if Hb is present in the stool and hydrogen peroxide in the test reagent. Sufficient quantities of blood any-

HE 20.3173/2:

where in the gastrointestinal tract can lead to a positive test. Results of several community screening programs and controlled trials are presented along with guidelines for use of the test. (18 Refs)

2. DETECTION OF GASTROINTESTINAL BLEEDING WITH 99MTC-LABELED RED BLOOD CELLS.

Winzelberg GG, McKusick KA, Froelich JW, Callahan RJ, Strauss HW

Div. Nuclear Medicine, Shadyside Hosp., 5230 Centre Ave., Pittsburgh, PA, 15232

Semin Nucl Med; 12(2):139-146 1982

Using a modified in vivo Tc-99m red cell labeling technique, gastrointestinal (GI) bleeding scintigraphy was performed in 100 patients with GI bleeding. Sixty-two patients with melena or bright red blood per rectum had positive scintiscans. In comparison to results of angiography, endoscopy, surgery and contrast radiography, radionuclide scintigraphy correctly located the site of bleeding in 83% of patients. The procedure could be performed over a 24 hr period which increased the sensitivity of the test since 85% of the scintiscans were positive at 1 hr or greater after the onset of imaging. The procedure was more sensitive than angiography in detecting sources of GI bleeding. We conclude that GI bleeding scintigraphy 99mTc-red cells is an accurate and effective method to detect upper and lower GI bleeding in patients with acute or intermittent gastrointestinal bleeding. (Author abstract) (13 Refs)

3. LOW DOWN GI BLEEDING.

Jeejeebhoy K

Univ. Toronto Fac. Medicine, Toronto, Ontario, Canada

Emerg Med; 14(7):207-209,213 1982

Lower gastrointestinal (GI) bleeding, whether mild or catastrophic, should always be attributed to colorectal disease, particularly colorectal cancer, until proven otherwise. Complete investigation of the causes of rectal bleeding is essential for all patients 40 yr old, especially those with iron deficiency anemia. Digital examination, proctosigmoidoscopy, air-contrast studies, and colonoscopy (including the cecum) are recommended. About 4% of older adults are believed to have intestinal polyps, which may be entirely asymptomatic or cause no symptom other than lower GI bleeding. Six consecutive negative fecal blood samples are needed before polyps can be ruled out with reasonable accuracy. Adenomatous and villous polyps are associated with synchronous neoplasms higher up in the GI tract in up to 30% of patients. Every polyp identified should be excised. The risk of malignancy is increased if the patient has a family history of malignancy, if the tumor involves the cecum or the sigmoid colon, if a polyp measures greater than 2 cm, or if air contrast studies show a 'dimple' at the base of the polyp. If cancer is present but the submucosa is not invaded, the cure rate after resection is 80-90%; if the lymph nodes are involved, the cure rate is 50%. Massive lower GI bleeding is more often caused by diverticular disease with erosion of a blood vessel, but eroding carcinomas, especially of the cecum (which are difficult to detect) can also cause massive GI bleeding. After the hemorrhage is controlled, the recommended diagnostic procedures are air contrast examination, colonoscopy, and if necessary an upper GI series. However, the cause of GI bleeding remains obscure in some 20% of patients. (no Refs)

4. EARLY PROLIFERATIVE CHANGES IN GASTROINTESTINAL NEOPLASIA.

Deschner EE

Lab., Digestive Tract Carcinogenesis, Memorial Sloan Cancer Center, 1275 York Ave., New York, NY, 10021

Am J Gastroenterol; 77(4):207-211 1982

The proliferative behavior of mucosal epithelium is reviewed in relation the development of gastrointestinal cancer. An enlarged proliferative compartment has been recognized among individuals with a previous history of colon cancer, those with an isolated polyp, asymptomatic relatives of familial polyposis patients, those with ulcerative colitis, and even some members of the general population. Mucosa of patients with a previous history of colon cancer may show both extension of the proliferative compartment to the luminal surface (Stage I defect) and a shift in the major zone of DNA synthesis from the lower third of the gland to the middle and upper portion of the crypt (Stage II defect). Studies of 1,2-dimethylhydrazine-induced colon carcinogenesis in mice indicate that Stage II abnormalities are predictive of the development of cancer. Distribution of DNA synthesizing cells among patients belonging to several high risk groups is presented. Only 30% of the patients showed a completely normal proliferative pattern. Changes in proliferative patterns over time are described for two asymptomatic members of polyposis coli families. Histologically normal mucosa from patients with a previous history of neoplasia may show crypts with extremely elevated labeling indices. The importance of such crypts is discussed. Correlation of an abnormal proliferative pattern with the type of tumor that will emerge is described. The impact of a diet rich in animal and dairy fats is considered. (16 Refs)

5. UNUSUAL ADENOMATOUS POLYPS IN JUVENILE POLYPOSIS COLI.

Mills SE, Fechner RE

Dept. Pathology, Univ. Virginia Medical Center, Box 214, Charlottesville, VA, 22908

Am J Surg Pathol; 6(2):177-183 1982

The histological findings in juvenile polyposis coli (JPC) in a 14-yr-old boy are compared with those in rectal polyps removed from the patient 25 yr later. The latter exhibited cytologic changes characteristic of adenomatous polyps but a peculiar architectural arrangement of the glands. Two other types of polyps that are associated with JPC and often designated as adenomas are also illustrated. The possibility that patients with JPC may be at increased risk for colonic carcinoma is discussed. (22 Refs)

6. SERUM LEVELS OF CARCINOEMBRYONIC ANTIGEN AND A TUMOR-EXTRACTED CARCINOEMBRYONIC ANTIGEN-RELATED ANTIGEN IN CANCER PATIENTS.

Shively JE, Spayth V, Chang FF, Metter GE, Klein L, Presant CA, Todd CW

Div. Immunology, City of Hope Res. Inst., Duarte, CA, 91010

Cancer Res; 42(6):2506-2513 1982

Levels of carcinoembryonic antigen (CEA) and a tumor-extracted CEA-related antigen (TEX) were determined in sera from patients with carcinomas of the breast, colon, lung, head and neck, and a number of miscellaneous categories. The purpose of this study was to compare the levels of each antigen at various stages of malignant disease. Competitive radioimmunoassays developed in our laboratory were shown to be sufficiently specific to detect either of these two antigens independent of each other. The results indicate that: (a) with our specific assays, CEA was not significantly elevated in smoker controls, but TEX was elevated in 29% of smoker controls; (b) TEX was equivalent to CEA as a tumor marker for colonic cancer. TEX was better than CEA as a marker for lung cancer and, based on limited data, there is a possibility that TEX is a significantly better tumor marker than is CEA in early lung cancer; (c) TEX was superior to CEA as a tumor marker for breast and head and neck cancers; (d) there is a strong indication that serial determinations of TEX can be used as effectively as CEA in the monitoring of disease progress. These preliminary results must be confirmed by increasing the number of cancer patients and including nonmalignant disease controls. (Author abstract) (18 Refs)

7. ULTRASTRUCTURAL LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL INTESTINE AND COLON CANCER. ABNORMAL DISTRIBUTION OF CEA ON THE SURFACES OF COLON CANCER CELLS.

Ahnen DJ, Nakane PK, Brown WR
(c/o Brown), Veterans Admin. Medical Center, 111E, 1055 Clermont St., Denver, CO, 80220
Cancer: 49(10):2077-2090 1982

The distribution of carcinoembryonic antigen (CEA) in normal small intestine, normal colon, and colon cancer of humans was determined immunocytochemically by the peroxidase-labeled antibody method at the light and electron microscopic levels. In the small intestine, CEA was found in protein synthetic organelles, in the mucus, on the microvilli of goblet cells, and on some microvilli of columnar cells adjacent to goblet cells. In the normal colon, CEA was found in protein synthetic organelles of the fully differentiated columnar cells and goblet cells, as well as on the microvilli of the cells. In two well-differentiated colon cancers, the normal preferential surface expression of CEA on the microvilli was maintained, but in six poorly differentiated cancers, CEA was distributed equally over the entire cell surface. We conclude that CEA is a product of goblet cells in the small intestine, columnar and goblet cells in the colon, and colonic cancer cells. CEA on the surfaces of the normal epithelial cells is expressed in a polar manner. This polarity is lacking in undifferentiated neoplastic colon cells, which suggests that failure to establish or maintain the polar expression of normal cell-surface glycoproteins is a characteristic of the neoplastic cells. (Author abstract) (51 Refs)

8. TISSUE CARCINOEMBRYONIC ANTIGEN, DYSPLASIA, AND DISEASE DURATION IN COLONIC INFLAMMATORY BOWEL DISEASE.

Greenstein AJ, Panvelliwalla DK, Katz LB, Heimann TM, Donnelly J, Pertsimlidis D, Geller S, Smith H, Aufses AH
Dept. Surgery, Mount Sinai Sch. Medicine City Univ. New York, New York, NY
Am J Gastroenterol; 77(4):212-215 1982

Tissue carcinoembryonic antigen (CEA) was studied in five groups of patients: 8 ulcerative colitis patients with mild or no dysplasia, 5 ulcerative colitis patients with severe dysplasia, 7 Crohn's disease patients with nondiseased colon, 9 Crohn's disease patients with diseased colon, and 18 colorectal cancer patients from the noncancerous colon resection margins. CEA levels were significantly lower in the normal colon Crohn's group than all other groups (p less than 0.05). CEA levels were significantly higher in the severe dysplasia ulcerative colitis group than all other groups (p less than 0.05). The Crohn's disease patients with diseased colon, the ulcerative colitis patients with mild or no dysplasia, and the colorectal cancer group with noncancerous colon all had similar intermediate CEA levels. (Author abstract) (26 Refs)

9. THE PRESENCE OF ONCOFOETAL ANTIGENS IN LARGE BOWEL CARCINOMA.

Ma J, De Boer WG, Nayman J
Dept. Lab. Medicine, Royal Southern Memorial Hosp., P.O. Box 185, Caulfield South, Victoria 3162, Australia
Aust NZ J Surg; 52(1):30-34 1982

This paper is an immunohistological study of the occurrence of the oncofetal antigens, carcinoembryonic antigen (CEA), small intestine mucin antigen (SIMA), and normal large bowel mucin antigen (LIMA) in 60 surgically resected colons: 10 non-malignant specimens and 50 colorectal carcinomas. SIMA is a new oncofetal antigen found in mucinous carcinoma of the large bowel. In the adult it is normally present only in the duodenum and jejunum. Of the 50 carcinoma specimens, 13 were mucinous, 17 non-mucinous and 20 mixed mucinous and non-mucinous. LIMA was the only antigen detected in the mucosa of non-malignant specimens. In mucinous carcinomas only SIMA was present, whilst in the non-mucinous specimens CEA was always found and to a lesser extent LIMA. The same relationship was observed in mixed tumors: SIMA in mucinous and CEA-LIMA in the non-mucinous parts. In the mucosa adjacent to the cancer in all 50 cases there was evidence of an increase or decrease in LIMA. In 42 cases (84%) both oncofetal antigens (CEA and SIMA) could also be detected in this transitional or perineoplastic epithelium at varying distances from the tumor. These results provide evidence to suggest that the majority of large bowel carcinomas occur in areas of metaplastic change. (Author abstract) (23 Refs)

10. RECTAL CARCINOIDS AS TUMORS OF THE HINDGUT ENDOCRINE CELLS: A MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL ANALYSIS.

O'Briain DS, Tischler AS, Dayal Y, Bendon R, DeLellis RA, Wolfe HJ
(c/o Wolfe) Dept. Pathology, Tufts Univ. Sch. Medicine, 136 Harrison Ave., Boston, MA, 02111
Am J Surg Pathol; 6(2):131-142 1982

A series of 13 human hindgut (rectal) carcinoid tumors was investigated for morphological features, peptide hormone content, and silver staining properties, and compared with normal rectal endocrine cells. Immunochemistry involved staining by peroxidase-antiperoxidase method followed by incubation with rabbit antibodies (antibovine pancreatic polypeptide (BPP), antihuman pancreatic polypeptide (HPP), antiglucagon (glucagon-like immunoreactivity, GLI), antisomatostatin (SRIF), antigastrin) and guinea pig anti-insulin 1. Overall, 85% of the tumors were positive, either by Grimelius (argyrophilia), immunohistochemical staining, or both. The hindgut carcinoids are similar to normal endocrine cells of the region; PP, GLI, SRIF, and other substances found in rectal carcinoids are also products of normal rectal endocrine cells. Secretory products of the multiple endocrine cell types indigenous to other gut areas are rarely if ever found in these tumors. These similarities strongly suggest a common origin of rectal carcinoids from normal rectal endocrine cells. The distinctive profile of hormonal and silver staining properties of rectal carcinoids has potential value at the cellular level as a specific marker of rectal or hindgut origin. (37 Refs)

11. THE ROLE OF ENZYMOLOGY IN DIFFERENT CONDITIONS OF COLON AND RECTAL MUCUS.

Bereznitsky S, Lobstein OE, Ko ST, Weinstock A

John J. Mack Res. Lab., Mt. Sinai Hosp. Medical Center, 2755 W. 15 St., Chicago, IL, 60608

Am J Proctol Gastroenterol Colon Rectal; 33(3):6,8,11 1982

Six enzymes widely used in serum as a diagnostic tool (amylase, lipase, CK, LD, AST, ALT) were assayed in colonic mucus obtained via colonoscope from 75 patients (including 12 without gastrointestinal tract disease) with different pathological conditions of the Colon and Rectum. The investigation demonstrates that the colonic mucosal layer is the site of tremendous metabolic activity. Measurement of enzyme activity in mucus reflects the character of inflammatory or destructive processes occurring in colonic mucosal cells. The selection of appropriate enzyme tests of diagnosis is not a simple matter. However, various combinations of enzyme tests do offer the possibility to describe pathogenesis of different diseases, including their use as a diagnostic tool in metabolic disorders of colonic mucosa. (Author abstract) (12 Refs)

12. TISSUE POLYPEPTIDE ANTIGEN - A NEW TUMOUR MARKER?

Wagner W, Husemann B, Becker H, Groitl H, Koerfgen HP, Hammerschmidt M

Surgical Clinic, Univ. Erlangen-Nurnberg, 8520 Erlangen, W. Germany

Aust NZ J Surg; 52(1):41-43 1982

The possibility of using Tissue Polypeptide Antigen (TPA) as a tumor marker in the diagnosis and follow-up of patients with malignant tumors was reported. We have taken up these suggestions and examined the possible role of TPA as a tumor marker in gastric and colo-rectal carcinoma. TPA and CEA (Carcinoembryonic Antigen) values were determined in 39 patients with gastric and 60 patients with colo-rectal carcinoma. The tumors were histologically proven. The histological classification of the gastric carcinomas was carried out according to the recommendations of the AJC (American Joint Committee for cancer staging and end results reporting) and that of the colo-rectal carcinomas was according to Dukes. Fifty-two surgical patients with benign diseases were used as controls. In this group the incidence of false positive values was 15.3% for TPA and 23% for CEA. In gastric carcinoma 30 out of 39 patients (76.9%) had on elevated TPA level (medium 275.4 n/l), in contrast CEA was elevated in 18 out of 35 patients (46.1%, medium 24.6 ng/ml). In colo-rectal cancer the TPA level was increased in 61.6% ie 37 out of 60 patients (medium 260.2 n/l). Elevated CEA levels were detected in 38 out of 60 patients (63.6%, medium 192 ng/ml). The mean values of TPA and CEA rise with advancing tumor stages. Elevated TPA levels were also found in non malignant diseases. Possible sources of error are inflammatory reactions. Therefore increased TPA values should be considered indicative of neoplasia only if infections or inflammatory diseases can be excluded and the first value is confirmed by repeated examination. The high incidence of increased values in early tumor stages (Dukes A or AJC 1), seems to justify the inclusion of tests for these antigens into the diagnostic and follow-up routine of gastric and colorectal cancer. (Author abstract) (9 Refs)

13. THE ROLE OF TENNESSEE ANTIGEN IN THE DIAGNOSIS OF GASTROINTESTINAL MALIGNANCY.

Sampson J, Wong L, Harris OD
(c/o Harris) Gastroenterology Dept., Princess Alexandra Hosp., Woolloongabba 4102, Queensland, Australia
Aust NZ J Surg; 52(1):39-41 1982

Tennessee antigen (TAG) is a glycoprotein which has been extracted from adenocarcinoma of the colon. It is one of the numerous tumor associated antigens which has been developed and there is evidence that it differs considerably from carcinoembryonic antigen (CEA) preparations. A commercial kit using a hemagglutination inhibition assay is available and its ability to discriminate between benign and malignant conditions of the gastrointestinal tract has been studied, using 7.7 units/ml as the upper limit of normal. With upper gastrointestinal disease, discrimination is comparable to that achieved with TAG by other workers and also to that achieved with CEA. For gastric carcinoma TAG has a sensitivity of 71% and a specificity of 77%. With lower gastrointestinal tract disease discrimination was poor, TAG having a sensitivity of 76% but a specificity of 44% for colorectal carcinoma. Discrimination between pancreatic carcinoma and chronic pancreatitis was poor, TAG having a sensitivity of 100% for carcinoma and a specificity of 22%. (Author abstract) (8 Refs)

14. LYMPHOCYTE FLUORESCENCE POLARIZATION CHANGES AFTER PHYTOHEMAGGLUTININ STIMULATION IN THE DIAGNOSIS OF COLORECTAL CARCINOMA.

Hocking GR, Rolland JM, Nairn RC, Pihl E, Cuthbertson AM, Hughes ES, Johnson WR
(c/o Nairn) Dept. Pathology and Immunology, Monash Univ., Alfred Hosp., Commercial Road, Prahran, Victoria 3181, Australia
JNCI; 68(4):579-583 1982

A lymphocyte fluorescence polarization test that measures reactivity to phytohemagglutinin (PHA) has permitted discrimination of a majority of patients with colorectal carcinoma from noncancer individuals. The test involves separation of two lymphocyte fractions from 20 ml venous blood on a modified leukocyte separation gradient, incubation with PHA for 45 min, addition of fluorescein diacetate, and analysis of change in fluorescence polarization. Of 19 colorectal patients tested preoperatively, 13 had a positive stimulation index, 3 a zero index, and 3 a negative index. Of seven patients with other malignant neoplasms, a positive value was obtained in six and a negative value in one. Of 14 patients with other diseases, a negative value was obtained in 9, zero in 3, and positive in 2. Of 31 normal donors a negative value was obtained in 27, zero in 2, and weak positive in 2. This rapid test promises to develop into a useful cancer-diagnostic method, and elucidation of its biological basis should identify a new cancer marker. (Author abstract) (22 Refs)

15. STAINING PROPERTY OF HUMAN COLONIC MUCIN BY PERIODIC ACID-THIONIN SCHIFF/POTASSIUM HYDROXIDE/PERIODIC ACID-SCHIFF (PAT/KOH/PAS) METHOD.

Muto T, Kamitani J, Konishi F, Sawada T, Sugihara K, Kusama S
Dept. Surgery, Univ. Tokyo Faculty Medicine, Tokyo, Japan
I To Cho; 17(3):343-348 1982

Staining of human colonic mucin was studied with respect to differences in staining properties of different diseased tissues (total 357 specimens) and their surrounding benign tissues. The four standard staining patterns that are observed with PAT/KOH/PAS (PKP) stain are as follows: blue, blue-purple, red-purple, and red. Except for 1 case each staining red or purple tubules in red, respectively, all 61 specimens of advanced carcinoma stained blue-red purple; this indicated abnormal mucin as suggested by Culling et al. Of the 39 adenomas, 23 stained red, 13 stained blue-red purple, and 3 stained purple tubules in red. Of the 11 villous or tubulo-villous adenomas, nine stained blue-red purple and one each stained red or purple tubules in red. Of the 74 specimens of background mucosa of the carcinomas, 47 stained blue-red purple, 21 stained red, and 6 stained purple tubules in red. Of the 40 specimens of background mucosa of adenoma, 21 stained blue-red purple, 14 stained red, and 5 stained purple tubules in red. The advanced carcinoma that stained red was within a mucosal adenoma and the carcinoma that stained as purple tubules in red was within a submucosal adenoma. Compared to the adenomas, the villous or tubulo-villous adenomas stained in a manner more like that of the carcinomas. Potential use of PKP staining for diagnosis of tumorous lesions of the colon and adenomatosis coli and for investigating the adenoma-carcinoma sequence was suggested. (6 Refs) (In JPN)

16. PATTERNS FOR NORMAL COLON MUCOSA AND COLON ADENOCARCINOMA COMPARED BY TWO-DIMENSIONAL GEL ELECTROPHORESIS.

Tracy RP, Wold LE, Currie RM, Young DS
Section Clinical Chemistry, Mayo Clinic, Rochester, MN, 55905
Clin Chem; 28(4,part2):915-919 1982

A two-dimensional gel 'map' of the proteins in normal cells and transformed cells may well help establish the presence of putative tumor-specific protein antigens, which can be isolated and used as antigens. We so examined normal colon mucosa and colon adenocarcinoma, using a sensitive silver stain. Samples were promptly prepared after excision by rapidly trimming the tissue to a small, grossly homogeneous piece, which was frozen on solid CO2. Frozen histological sections and permanent mounts were also prepared for several areas, to document the cellular constitution and to grade the carcinoma. Sample preparation for electrophoresis is described. The DNA was pelleted by centrifugation (108,000 X g X 1.5 hr). Little or no pellet was observed, indicating complete solubilization. Many of the tumors contained proteases, liberated during sample preparation, so protease inhibitors were included. A highly reproducible pattern was observed for normal mucosa. Comparison of the gels from paired samples with histological data allows many of the spots to be tentatively assigned to the different cell types present in the mucosa (epithelium, connective tissue, or muscularis mucosa) and, in most tumors analyzed, detection of a series of spots that are not detectable in the pattern for normal tissue. These apparently tumor-associated proteins may be of epithelial cell or stromal origin. (Author abstract) (13 Refs)

17. TWO-DIMENSIONAL ELECTROPHORETIC PATTERNS OF PROTEINS OF NORMAL MUCOSA, POLYPS, AND CARCINOMAS OF THE LARGE INTESTINE.

Thorsrud AK, Vatn MH, Jellum E
(c/o Jellum) Inst. Clinical Biochemistry, Rikshospitalet, Oslo 1, Norway
Clin Chem; 28(4,part2):884-889 1982

Two-dimensional protein maps of biopsies from normal mucosa, tubular adenomas (polyps), and colonic carcinomas in humans have been studied in order to obtain information on the possible precancerous role of intestinal polyps. The maps are complex and several hundred protein spots are seen after staining with Coomassie Blue. Most of the spots are common to these three tissue types, but there are also differences. Polyps and carcinomas had a strikingly similar protein pattern, different from that of normal mucosa. There were negligible differences in the two-dimensional protein maps of tubular adenomas from patients who also had colonic cancer, as compared with adenomas from persons without carcinomas. The results lend further support to the hypothesis that polyps may be precursors of carcinomas of the large intestine. (Author abstract) (15 Refs)

18. COLONIC ABSORPTION OF SECONDARY BILE-ACIDS IN PATIENTS WITH ADENOMATOUS POLYPS AND IN MATCHED CONTROLS.

van der Werf SD, Nagengast FM, Van Berge Henegouwen GP, Huijbregts AW, Van Tongeren JH
Municipal Hosp., Wagnerlaan 55, 6815 AD Arnhem, The Netherlands
Lancet; 1(8275):759-762 1982

Colonic absorption of deoxycholate and the proportion of secondary bile-acids in duodenal bile were significantly higher in 11 patients with adenomatous polyps than in 11 controls matched for age, sex, and gut transit time. In the patients with adenomas the large bowel made a greater contribution to bile-acid conservation, and this was associated with a more rapid turnover of cholic acid, but not with the adenoma patients' higher consumption of cholesterol. These data accord with the hypothesis that bacterially degraded bile-salts are involved in the adenoma-carcinoma sequence of the colon. (Author abstract) (33 Refs)

19. LACK OF CORRELATION BETWEEN METASTASIS OF HUMAN RECTAL CARCINOMA AND THE ABSENCE OF STROMA FIBRONECTIN.

Niemczuk P, Perkins RM, Talbot IC, Critchley DR
(c/o Critchley) Dept. Biochemistry, Univ. Leicester, Leicester LE1 7RH, England
Br J Cancer; 45(4):500-505 1982

In a retrospective study we have used an immunoperoxidase procedure to localize the glycoprotein fibronectin in human rectal carcinomas, concentrating on tumor invading thick-walled extramural veins. Fibronectin was present in 29 out of 38 cases, in connective tissue stroma, and was not in direct association with the tumor cells, except in areas of necrosis. We found no correlation between the presence or absence of stromal fibronectin and (1) the degree of cellular differentiation within the tumor, (2) tumor progression (Dukes' classification) (3) the subsequent development of metastases and (4) patient longevity. Our results do not support the conclusions from in vitro studies that the metastatic potential of carcinomas may be partly determined by the ability of tumor cells to synthesize pericellular fibronectin. (Author abstract) (31 Refs)

20. HETEROGENEOUS RESPONSE TO X-RAY AND ULTRAVIOLET LIGHT IRRADIATIONS OF CULTURED SKIN FIBROBLASTS IN TWO FAMILIES WITH GARDNER'S SYNDROME.

Kinsella TJ, Little JB, Nove J, Weichselbaum RR, Li FP, Meyer RJ, Marchetto DJ, Patterson WB

Radiation Oncology Branch, Div. Cancer Treatment, NCI, NIH, Building 10, Room B3-B38, Bethesda, MD, 20205

JNCI; 68(5):697-701 1982

A heterogeneous response to x-ray and far UV (254 nm) light irradiations was found in cultured skin fibroblast lines from two separate families with Gardner's syndrome. When compared to two normal control cultures and cultures from two patients with nonfamilial colon cancer, cultures from four clinically affected members of Family 1 showed increased sensitivity to the lethal effects of both x-ray and UV light irradiations. These cell lines also showed a delayed pattern of x-ray potentially lethal damage repair (PLDR) and absent UV PLDR. In contrast, cultures from three members of Family 2 (2 of whom were clinically affected) showed a normal response of survival and PLDR to both x-ray and UV light irradiations. Thus increased sensitivity of cultured skin fibroblasts to x-ray and UV light irradiations was not a consistent in vitro finding in patients with Gardner's syndrome. However, in families with Gardner's syndrome who demonstrate in vitro radiosensitivity, additional studies are needed to assess the usefulness of these techniques in detecting affected individuals prior to the development of colon carcinoma and other manifestations. (Author abstract) (29 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

21. SURGICAL EXPERIENCE WITH CARCINOMA OF THE COLON AND RECTUM.

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Ann Surg; 195(5):600-607 1982

From September 1925 through December 1978 at Vanderbilt University Hospital, 1,279 patients with adenocarcinoma of the colon and rectum underwent operations. Reports of this cumulative series have been published previously; the last report in 1970 included 1,022 patients. The current report examines the progress made in our recognition and management of colorectal cancer. During this 54-yr period, there has been a relative decrease in the incidence of carcinoma of the rectum and a relative increase in carcinomas elsewhere in large bowel. Resectability rate has steadily increased, culminating in a rate of 98.4% in the recent period (1969-1978). The operative mortality rate fell to 4.3% (1956-1960) but has shown a slight rise to 5.4% in the recent period (1969-1978). This reflects the increased number of patients in the 8th to the 10th decades of life. Five-yr survival rates in 99% of 1,218 patients were computed. Absolute 5-yr survival for the recent period was 43.7%, compared with 17% for the initial period. Five-yr survival rates for patients in the recent decade with Dukes A, B, and C lesions were 67%, 58.6%, and 33.3%, respectively. Comparison of survival data in the last two decades shows little improvement. However, in the last 20 yr, 78-80% of patients had more advanced lesions. (Author abstract) (19 Refs)

22. ANAL CANCER IN DENMARK DURING THE PERIOD 1943-1973. I. SQUAMOUS-CELL CARCINOMA OF THE ANUS: DIAGNOSIS, TREATMENT AND PROGNOSIS.

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Ugeskr Laeger; 144(12):851-856 1982

One hundred and seventy-six patients in whom squamous-cell carcinoma of the anus was diagnosed during the period 1943-1973 were followed up. Sixty-nine of the 176 tumors were localized in the perianal region and 107 in the anal canal. Hemorrhage from the anus, pain and sensation of distension were the most frequent symptoms of cancer. One hundred and twelve patients were subjected to surgery: 51 to tumor excision, 48 to abdominoperineal rectal extirpation, 17 to abdominoperineal rectal extirpation with vaginectomy, 5 to abdominoperineal rectal extirpation with lymphadenectomy, 3 to colostomy and 5 to tumor excision with lymphadenectomy. Surgery was combined with radiotherapy in 32 patients, and 12 patients were subjected to radiotherapy only. Three patients were not treated at all. Recurrences were seen in 64.7% of the 51 patients (31 with perianal tumors and 20 with tumors of the anal canal) after presumed radical excision, and 39% of the patients with recurrences died of the tumor. The incidence of recurrence was 31.3% of 48 patients subjected to presumed abdominoperineal rectal extirpation. Recurrences were seen in 17.6% of 17 women subjected to rectal extirpation with vaginectomy. The crude 5-yr survival rate was 52.4% for the 176 patients. The prognosis was best for patients with small superficial perianal tumors and for those without lymph node metastases. At the time of reporting 53.3% of the patients without and 17.6% of those with lymph node metastases were tumor-free, and 10.3% and 8.8%, respectively, were alive with tumors. (12 Refs) (In DAN)

23. CARCINOMA OF RECTUM: RESULTS FOLLOWING SURGICAL RESECTION 1971-1979.

Chapuis PH, Pheils MT, Newland RC, Smyth E, Dent O, Bokey EL, Payne JE

Dept. Surgery, Univ. Sydney, Concord Hosp., Clinical Sciences Building, Concord 2139, Australia

Aust NZ J Surg; 52(1):16-23 1982

Comparison of 122 patients who have had an abdominoperineal excision of the rectum with 118 patients treated by conventional anterior resection showed no significant difference in patient survival. The grounds were comparable in respect of age, sex, tumor level and pathology. This suggests that conventional restorative resection for rectal cancer may be undertaken without adversely affecting survival. (Author abstract) (21 Refs)

24. INDICATIONS FOR SURGICAL TREATMENT OF RECURRENT COLORECTAL NEOPLASMS AND THEIR METASTASES.

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Helv Chir Acta; 48(6):873-878 1982

Surgical treatment of recurrences of colorectal neoplasms (CRN) detected due to elevated blood carcinoembryonic antigen (CEA) levels and of pulmonary and hepatic metastases is discussed. Results of surgical treatment of CRN recurrences and metastases have been poor due to late presentation and nonspecificity of symptoms. Prior to surgery, measurement of

CEA levels is of little diagnostic importance in CRN due to its lack of specificity. Following surgery, increases in CEA levels are indicative of CRN recurrence. In CRN patients with preoperative elevation of CEA, absence of postoperative decrease is associated with a poor prognosis. The mean survival for patients with liver metastases of CRN is 8 mo, although it is doubled in the case of solitary metastases. No evidence exists to suggest that surgical treatment of the CRN liver metastases significantly prolongs survival. Pulmonary metastases of CRN usually occur in later stages and rarely are isolated, usually accompanied by local recurrence, liver metastases, and other sites of involvement. (21 Refs) (In FRE)

25. METASTATIC DISEASE IN THE LIVER FROM COLORECTAL CANCER: AN APPRAISAL OF LIVER SURGERY.

Bengmark S, Hafstrom L, Jeppsson B, Jonsson PE, Ryden S, Sundqvist K
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World J Surg; 6(1):61-65 1982

Thirty-two patients with colorectal cancer underwent liver resection; 12 had solitary liver metastases, 16 had two or more, and the number was unrecorded in 4. In seven patients, enucleation of one or two solitary liver metastases was performed. Eighteen of the patients had synchronous metastases and 14 had metachronous metastases. Of the patients enucleated, metastases were synchronous in six and metachronous in one. The median interval between primary cancer and surgery in patients with metachronous metastases was 16 mo, mean 30 mo. Median survival of the 18 resected patients with synchronous metastases was 21 mo (mean 27 mo), and of the 12 resected patients with metachronous metastases 16.5 mo (mean 20 mo). Median survival of the 12 patients with a single metastasis was 25 mo (mean 33, range 11-102), and for the 16 with two or more metastases it was 17 mo (mean 19, range 3-71). Of the patients treated by enucleation, three were still alive at 40, 41, and 108 mo, and four died at 2, 3, 28, and 65 mo, respectively, postoperatively. Complications occurred in 10 patients overall, including 2 deaths. Cytostatic therapy was given to 18 patients. Overall, nine patients survived greater than 3 yr. Liver resection or metastasis enucleation may be useful in patients with colorectal cancer and liver metastases when the number of metastases is limited and no extrahepatic cancer is present. (25 Refs)

26. THE TRANSSPHINCTERIC APPROACH TO RECTAL VILLOUS ADENOMAS.

Heij HA, Tan KG, Van Houten H
Dept. General Surgery, Univ. Hosp. Dijkzigt, Rotterdam, The Netherlands
Neth J Surg; 34(1):4-7 1982

Six cases of rectal villous adenomas in which a transsphincteric approach allowed complete excision in the submucosal layer with preservation of the anal sphincter are presented. Two patients presented with a recurrence, one after previous local excisions and the other after a previous low posterior resection. All but one patient had extensive, sessile, carpet-like tumors. Histologic analysis of one patient indicated the possibility of malignancy, although none was detected at subsequent operation. The other five patients had adenomas with varying degrees of atypia without invasive features. In three of these patients the remaining mucosal defect was left open, and in two a defunctioning colostomy was performed. No serious complications occurred and all incisions healed primarily without infection or fistulae. During the follow-up period (6-21 mo) two recurrences were seen which were excised transanally. This approach to sessile rectal villous adenoma is a valuable aid in the management of these tumors. A colostomy is apparently not routinely indicated when defects greater than 7 cm are left unsutured, provided a bland diet is given postoperatively. (18 Refs)

27. ENDOSCOPIC INTERVENTIONS IN VILLOUS COLONIC TUMORS.

Strekalovskii JP, Kuz'min AI, Kapuller LL, Ezhova GI, Khakhanova MV
Res. Inst. Proctology, Moscow, USSR
Vestn Khir; 128(2):37-42 1982

Of 1,070 patients subjected to endoscopic removal of colonic neoplasms, 103 had villous tumors. A total of 112 tumors were removed. The size of villous tumors ranged from 2 to greater than 6 cm. The tumors were located in the rectum (10), sigmoid colon (66), descending colon (7), transverse colon (17), and cecum and ascending colon (12). Nine patients had multiple tumors, and 50 had villous tumors in combination with the polyps. The multi-stage endoscopic interventions were the treatment of choice. The intervals between endoscopies depended upon the size of the tumor and the type of tumor growth. Histological examination of tumor specimens showed 28 glandular-villous polyps without malignant transformation, 14 villous-glandular polyps with malignant transformation, 56 villous adenomas without malignancy, and 14 villous adenomas with malignant transformation. Of 78 patients followed up for 1-7 yr after the endoscopic removal, 56 were free of disease, 13 developed a recurrence, 5 showed continuous tumor growth, and 4 developed cancer. (2 Refs) (In RUS)

28. EXPERIENCES AND RESULTS WITH THE MECHANICAL ANASTOMOSIS OF THE COLON AND RECTUM COMPARED TO THE CONVENTIONAL DOUBLE-ROW TECHNIQUE.

Muller M, Krumme H, Gumrich H
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Aktuel Chir; 17(1):13-18 1982

Results of colorectal anastomosis are compared in 46 patients treated mechanically using a staple gun and 50 patients treated by the manual technique. The mechanical method is equal or superior to the manual method. The staple gun provides better results in adipose patients and patients with narrow pelvises. The staple gun saves time, reducing the surgical burden to the patient. Use of a large-diameter stitching head reduces the risk of stenosis. (18 Refs) (In GER)

29. 100 CONSECUTIVE COLON RESECTIONS USING MODIFIED SINGLE-ROW SUTURING.

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Chirurgische Klinik, Kantonsspital, CH-4410 Liestal, Switzerland
Helv Chir Acta; 48(6):833-837 1982

Resection of the colon using a modified single-row suture technique was performed on 100 consecutive patients with benign or malignant tumors or ulcerative colitis. Preoperative complications (perforation of the colon, peritonitis, ileus, and bleeding) were present in 39% of cases. Overall mortality was 1%. Successful anastomosis without colostomy was achieved in 98% of cases. Leakage of the anastomosis occurred in two cases but healed without further surgery. (7 Refs) (In GER)

30. A COMPARISON OF INTRAVENOUS AND ORAL METRONIDAZOLE AS PROPHYLACTIC IN COLORECTAL SURGERY.

Beggs FD, Johanputra RS, Holmes JT
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Br J Surg; 69(4):226-227 1982

In a prospective randomized double-blind trial we have compared oral (n = 46) and parenteral prophylaxis (n = 51) with metronidazole in elective colonic resection. All patients received oral or iv metronidazole, together with oral neomycin. The overall infection rate was 11.3%. Six out of 46 patients in the oral group (13%) had a wound infection postoperatively compared with 5 out of 51 patients who received iv metronidazole (9.8%). These results suggest that there is no significant difference whether metronidazole is administered iv or orally as a prophylactic in elective colonic surgery. (Author abstract) (10 Refs)

31. COMBINED ADJUVANT THERAPY OF RADICALLY OPERATED COLORECTAL CANCER PATIENTS. (CHEMOTHERAPY, RADIOTHERAPY, AND MER-BCG).

Robinson E, Bartal A, Cohen Y, Haim N, Mohilever J, Mekori T
Dept. Oncology, Nothern Israel Oncology Center, Rambam Medical Center, Haifa 35245, Israel
Cancer Chemother Pharmacol; 8(1):35-40 1982

Long-term follow-up of 73 patients who had undergone curative surgery for colorectal cancer and adjuvant therapy is reported. Patients were randomized into groups to be treated with radiochemotherapy (RC) or RC plus methanol extraction residue of BCG (RCM). Forty-four patients had Dukes' C colorectal cancer (DCC) and 29 Dukes' B2 rectosigmoid cancer (DRC). The major characteristics of these patients are summarized. The RCM and RC subgroups were similar, except that in Stage B2 the female/male ratio was higher in the RC-treated than in the RCM-treated patients. The actuarial survival (AS) at 54 mo was 78% in the RCM subgroup and 26% in the RC subgroup. The difference was statistically significant. At 54 mo the difference in AS was no longer significant (53% for the RCM-treated and 25% for the RC-treated patients). In DRC patients, the AS at 42 mo was significantly better in the RCM-treated patients than in those treated with RC. In DCC of the proximal colon a better survival at 54 mo was obtained in nine patients treated with 5-fluorouracil (5-FU) and methanol extraction residue of BCG than in eight patients treated with 5-FU alone. The survival and disease-free interval at 48 mo in DRC patients were 55% and 46%, respectively, for the RCM-treated patients and 61% and 31% in RC-treated patients. In patients with DCC, the disease recurred in 8 (36.4%) of the RCM group and in 12 (54.5%) of the RC group. In patients with DRC, recurrence developed in six (46.2%) RCM-treated patients and in six (37.5%) RC-treated patients. (32 Refs)

32. COMBINED TREATMENT OF RECTAL CANCER.

Fedorov VD, Kiseleva ES, Odareva TS, Sevost'ianov SI, Fridkina TV, Kapuller LL, Kovel' TA, Sadovnichii VA
Res. Inst. Proctology, Moscow, USSR
Vestn Khir; 128(2):42-47 1982

The efficacy of combined treatment was evaluated in 363 patients with cancer of the rectum. Group 1 (190 patients) underwent preoperative intensive radiotherapy (400 rads/day, for 5 days, total dose 2,000 rads) followed by surgery. Group 2 (173 patients) received surgery alone. Radical surgery was performed in 158 patients in Group 1 and in 159 patients in Group 2. Laparotomy or palliative surgery was performed in 32 patients in Group 1 and in 14 patients in Group 2 (these patients had liver metastases). Abdominal-perineal extirpation of the rectum was carried out in 110 patients in Group 1 and in 76 patients in Group 2; 48 in Group 1 and 83 in Group 2 were subjected to abdominal-anal resection. Postoperative lethality was 6% in Group 1 and 5% in Group 2. The 3-yr survival rates in Groups 1 and 2 were 73% and 75%, respectively. Local recurrences were observed in 6.7% of the patients in Group 1 and in 10% of the patients in Group 2. (25 Refs) (In RUS)

33. DEFINITIVE TREATMENT OF CARCINOMA OF THE ANUS WITH CHEMOTHERAPY AND RADIATION (MEETING ABSTRACT)

Flam MS, John M, Lovalvo L, Ager P
Fresno Community Hospital and University of California San Francisco, Medical Center San Francisco, CA
Proc Am Soc Clin Oncol; 1:C-375 1982

Eleven patients with cloacogenic (5) and squamous cell (6) carcinoma of the anus ranging in age from 40 to 89 years were treated with combined chemotherapy (CT) and radiotherapy (RT) in lieu of abdominal-perineal resection. Two courses of 5 FU (5-fluorouracil) (1000 mg/m(2)/day x 4 days) by continuous intravenous infusion and Mitomycin-C (10-15 mg/m2 IV bolus on day 1 of each course) were given 3-4 weeks apart simultaneously with whole pelvis RT to 3-4000 R. One patient received an additional tumor volume dose of 3000 R by interstitial iridium implant and one patient received a boost of 1000 R Orthovoltage to adjacent skin. Two of 11 patients were treated for local recurrance following surgical excision. All patients completed treatment. Substantial regression of the anal mass occurred by the end of the treatment course but a palpable residual abnormality was noted in all patients. Biopsies of the anal region performed on all patients between 1-5 months after completion of therapy revealed fibrosis and/or chronic inflammation and no evidence of residual cancer. Ten of 11 patients are alive without evidence of disease 4-19 months (median 9.5 months) after completion of treatment. One patient died 9 months after diagnosis of pulmonary embolism and was tumor free at autopsy. All patients developed moderate to severe proctitis and moist perineal desquamation. The patient who received an iridium implant developed a chronic anal ulcer after biopsy. Acute transient toxicity included stomatitis, leukopenia, thrombocytopenia and alopecia. (no Refs)

34. RADIATION +/- CHEMOTHERAPY (INTRAARTERIAL VS INTRAVENOUS) FOR LIVER TUMORS: AN NCOG PHASE III STUDY (MEETING ABSTRACT)

Friedman MA, Phillips TL, Carter SK, Sonoda T, Hanningan JF
University of California, San Francisco, CA, 94143
Proc Am Soc Clin Oncol; 1:C-359 1982

To compare the clinical value of whole liver radiation (RT) with or without simultaneous intravenous (IV) or hepatic intraarterial (IA) chemotherapy (CT), we treated 119 patients with hepatic tumors. All patients received RT (300 rad/day x 7) with or without CT consisting of Mitomycin C 8mg/m2 x 1 and Adriamycin 3mg/m(2)/d x 7 and 5-fluorouracil (5-FU) 10mg/kg/d x 8 continuous infusion. Patients were stratified, randomized and balanced according to performance status, prior chemotherapy, serum bilirubin and site of disease. Currently, 96 patients are evaluable: 47 colon, 24 hepatoma, and 25 other. Objective responses were judged at 4-6 weeks following therapy. Symptomatic benefit was achieved frequently: 76%

had pain relief and 70% nausea + vomiting relief. Hematologic toxicity was slightly less with RT alone, but overall only 3 patients had WBC less than 1000 and 10 had platelets less than 25,000. Currently we conclude for patients with hepatic tumors that: 1) RT + CT is superior to RT alone for induction therapy. 2) IA CT as employed in this study is not statistically superior to IV CT and is more cumbersome and expensive. (no Refs)

35. PHASE I STUDY AND PHARMACOKINETICS OF CIS-1,1,DI(AMINOMETHYL)-CYCLOHEXANE PT II SULPHATE (TNO-6) (MEETING ABSTRACT)

Pinedo H, Huinink TB, Simonetti G, Gall H, Van der Vijgh W, Canetta R, Van Putten L, Vermorken J, McVie G
Free University Hospital, Amsterdam 1081 HV, The Netherlands
Proc Am Soc Clin Oncol; 1:C-126 1982

The platinum analog TNO-6 shows similar activity against murine tumors as cisplatin (CDDP). There is evidence for a lack of cross resistance with CDDP. Animal toxicology showed less renal toxicity but more myelosuppression with TNO-6 than CDDP. TNO-6 was given in D5W as a 10 min IV infusion without hydration. Plasma kinetics and urinary excretion of platinum were compared with those of CDDP. Twelve patients (3 males, 9 females) received 2.5-25 mg/m2 q 3 wks. Patients characteristics were: age 56 yrs (median) 27-72 yrs (range); performance status 80 (50-90); prior radio-and/or chemotherapy 12; prior CDDP 8; courses per dose level 1-8; courses per patient 1-7. Toxicity included nausea and vomiting (11) diarrhea (2), constipation (1), dry mouth (2), dizziness (2) and neuropathy (1). Above 20 mg/m2 thrombocytopenia was observed, which was cumulative. We observed one complete remission of breast cancer (lung metastasis) and a minor regression of CDDP-resistant ovarian cancer. Stable disease was seen in ovarian (2) and colon (1) cancer and sarcoma (1); progressive disease in melanoma (1), and ovarian (2), breast (1), lung (1) and cervical cancer (1). Kinetic parameters after TNO-6 were: half-life alpha 6.2 min, half-life beta 3.4 days, Vc 5.8 l, Vd 18.4 AUC (area under the curve) 729 mg Pt/m2, B/mg Pt/m2 0.094, and cumulative 3-day urine excretion 27.9%. The data show different pharmacokinetics for TNO-6 and CDDP. (no Refs)

36. PHASE II EVALUATION OF DIHYDROANTHRACENEDIONE (DHAD, NSC 301739) IN PATIENTS WITH METASTATIC COLORECTAL CANCER (MEETING ABSTRACT)

Bedikian AY, Stroehlein JR, Korinek J, Karlin DA, Bodey GP
M. D. Anderson Hospital, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-368 1982

Phase II evaluation of DHAD was undertaken in 31 patients (pts) with colorectal cancer who had been previously treated with 5FU (5-fluorouracil) containing regimens. Of the 30 pts evaluable for tumor response, 27 had a good performance status (Zubrod 0 or 1). The starting dose of DHAD was 4 mg/m(2)/day given intravenously over 1 hour daily for 5 days q 4 weeks. Pts who had received prior treatments (Rxs) with mitomycin C or a nitrosourea compound received DHAD at dose of 3 mg/m(2)/day. There were no partial or complete responses. Stabilization of disease lasting 3 to 5 months occurred in only 8 pts. Progressive disease was noted in 22 pts. Dose limiting toxicity was neutropenia. There was a direct correlation betwen preexisting abnormal liver function tests and myelosuppression. A platelet count nadir of less than 100,000 was observed in 53% of the 30 Rxs with liver impairment compared with 24% of 38 Rxs without liver impairment. Other toxic reactions were mild to moderate. Generalized malaise and anorexia were common, occurring in 55% and 44% of the Rxs, respectively, Nausea, vomiting and diarrhea occurred during less than a fourth of the Rxs and usually were mild. Diarrhea was twice as common during Rxs given to pts with abnormal liver functions than to pts with normal liver functions (46% vs 21% of Rxs respectively). (no Refs)

37. METRONIDAZOLE (MR) WITH CHEMOTHERAPY: CLINICAL STUDIES (MEETING ABSTRACT)

Stewart DJ, Maroun JA, Young V, Crook AF, Tulloh M
Ontario Cancer Foundation Clinic, Ottawa, Ontario, Canada
Proc Am Soc Clin Oncol; 1:C-39 1982

Since nitromidazoles enhance many chemotherapy agents, we combined each of Adriamycin (A) 35-90 mg/m2 q 3 wk, BCNU (carmustine, B) 145-265 mg/m2 q 6 wk and mitomycin-C (MC) 10-20 mg/m2 q 6 wk with MR 1.5 g/m2 po 18 and 1 hr before and 6 and 24 hr after chemotherapy. Appropriate doses for phase II combinations with MR were found to be A 75 mg/m2, B 240 mg/m2, and MC 17 mg/m2. Nausea was moderate to severe, and potentiated by MR. Other toxicities with A were radiation-recall (1 patient), stupor (1), mucositis (4), cystitis (1), septicemia (2, 1 fatal). Five patients got A greater than or equal to 425 mg/m2 with no cardiotoxicity. Other toxicities with B were fatal thrombocytopenic bleeding (1), flushing (2), phlebitis (1), pseudomembranous colitis (1), hypotension (2). Three patients receiving MC had possible pulmonary toxicity (1 fatal). Numbers of tumors responding/stabilized/progressing were: a) on A: pharynx 1/1/0, salivary 2/0/0, squamous and adeno lung 1/1/0, pancreas 0/1/1, anus 0/0/1, breast 0/1/0, sarcoma 0/1/0, b) on B: glioblastoma 2/1/3, glioma 1/1/1, medulloblastoma 1/0/0, squamous and adeno lung 1/0/4, colon 0/1/1, parotid 0/0/1, melanoma 0/0/1, adeno unknown 0/0/1, c) on MC: breast 0/4/4, gastrointestinal 0/7/7, adeno lung 1/0/0, small cell lung 0/0/2, pharynx 0/0/2, parotid 0/0/1, anus 0/0/1, hepatoma 0/0/1, renal cell 1/0/0. Of note, 3 of 7 adeno and squamous lung cancers responded to MR combinations. (no Refs)

38. PHASE II TRIAL OF LOW DOSE METHOTREXATE AND SEQUENTIAL 5-FLUOROURACIL IN THE TREATMENT OF METASTATIC COLORECTAL CARCINOMA (MEETING ABSTRACT)

Kemeny N, Michaelson R
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Soc Clin Oncol; 1:C-370 1982

Preliminary studies in some solid tumors, including colorectal carcinoma suggest enhanced activity with high dose MTX (methotrexate) and sequential 5-FU (5-fluorouracil). We decided to test a low dose regime of MTX with a longer time interval -24 hours. Twenty-three previously untreated patients with measurable metastatic colorectal carcinoma were treated with MTX 40 mg/m2 IV day 1 followed by 5-FU 600 mg/m2 24 hours later on day 2. Treatment was repeated on day 8 and 9. Cycles were repeated every 28 days. There were 15 males and 8 females. The median Karnofsky PS was 80 (range 60-90) and the median age was 63 years (range 49-76). Indicator lesions were malignant hepatomegaly in 16 patients, lung in 7, lymph nodes in 1 and rectal masses in 2. Hematological toxicity was minimal; one patient had a WBC nadir less than 3000 cells/mm3. The major toxicity was mucositis noted in 60% of patients and a dose reduction was required in 5. Other side effects were mild abdominal pain in 30%, diarrhea in 26%, weakness in 19%, vomiting in 13%, hair loss in 13% and burn-ing in the eyes in 9%. Eight patients, 34% achieved a partial remission and 4 patients (17%) had a minor response. (1 Ref)

39. SEQUENTIAL THERAPY WITH METHOTREXATE (MTX) AND 5-FLUOROURACIL (5FU) FOR ADENOCARCINOMA OF THE COLON (MEETING ABSTRACT)

Blumenreich MS, Woodcock TM, Allegra MG, Richman SP, Kubota TT, Allegra JC
University of Louisville, Louisville, KY, 40292
Proc Am Soc Clin Oncol; 1:C-398 1982

In in vitro experiments, MTX administered prior to or simultaneously with 5FU is more effective than following 5FU. The proposed mechanisms are a) by increased cell uptake of 5FU or b) by increased binding of fluorodeoxyuridylate to thymidylate synthetase. Experiments with normal human marrow have shown no such increase in the uptake of 5FU, suggesting that such a combination may result in an increased therapeutic index. To test this hypothesis we treated 5 female and 4 male patients (pts) previously untreated with biopsy proven adenocarcinoma of the colon. The median age was 67. Seven pts had bidimensionally measurable metastatic disease: 5 in the liver, one in the lung and one in both. Three pts had metastatic disease found during laparotomy, and were started on chemotherapy in the postoperative period. Four pts had documented recurrence after 2, 11, 12 and 18 months (mos). The diagnosis and initial surgery in all cases was done within a month from the onset of symptoms; chemotherapy was started within one month of surgery. MTX was given at 200 mg/m2 followed one hour later by 5FU 600 mg/m2, both iv push; citrovorum 10 mg/m2 PO every 6 hours for 6 doses was started 24 hour after MTX. In no case were objective responses documented. Two patients have stable disease after 2 and 3 mos of therapy. Five patients progressed after 4.2 mos. The two pts started in an adjuvant manner are without evidence of recurrence at 8 and 12 mos after surgery and continue on therapy. Eighty-four courses of chemotherapy were given. Treatment was well tolerated. Toxicities were: Mild nausea and vomiting in 4 pts, diarrhea in 2, mucositis in 1, leukopenia in 1, serum creatinine above 1.5 mg/dl in 2 occasions. (no Refs)

40. PHASE I PILOT STUDY USING 24 HOUR SEQUENCED METHOTREXATE AND 5-FLUOROURACIL (MEETING ABSTRACT)

Benz C, Tattelman E, Cadman E
Yale University School of Medicine, New Haven, CT, 06510
Proc Am Soc Clin Oncol; 1:C-49 1982

Previous studies in breast, colon, and head and neck cancer have indicated some benefit to 1-4 hr sequencing of methotrexate (MTX) and 5-fluorouracil (FUra). However, in vitro studies in human carcinoma cell lines suggest optimal tumor toxicity is achieved when greater than 0.1uM MTX precedes FUra by 12-24 hr. A phase I study was begun to assess whether 24 hr sequenced MTX-FUra with leucovorin rescue (LV) could be tolerated. We wished, also, to determine if oral MTX would sustain serum concentrations of greater than or equal to 0.1uM over 24 hr. Seven patients were treated with 21 courses of therapy: MTX 50mg/m2 po q 6 hr x 5; FUra 600 mg/m2 iv x 1 at 1 hr post 5th dose MTX. All patients had received prior MTX and 6/7 had been previously treated with 1 hr sequenced MTX-FUra (+LV). Performance status in 6/7 patients was greater than or equal to 2; no patient was entered with neutropenia or creatinine clearance less than 65 ml/min. Four of 7 patients received greater than 2 courses at an average interval of 23 days between courses. Serum MTX levels were measured during all 21 courses of therapy: mean concentrations 1 hr prior to 5th dose MTX equals 1.07 +/- .74uM; 1 hr post 5th dose equals 2.10 +/- .92uM. In summary, this therapy appears to be well tolerated and a phase II study comparing 1 hr and 24 hr sequenced MTX-FUra appears warranted. (no Refs)

41. BIOCHEMICAL MODULATION OF ANTINEOPLASTIC RESPONSE IN COLORECTAL CARCINOMA: 5-FLUOROURACIL (F), HIGH DOSE METHOTREXATE (M) WITH CALCIUM LEUCOVORIN (L) RESCUE (FML) IN TWO SEQUENCES OF ADMINISTRATION (MEETING ABSTRACT)

Mehrotra S, Rosenthal CJ, Gardner B
Downstate Medical Center, Brooklyn, NY, 11203
Proc Am Soc Clin Oncol; 1:C-387 1982

We conducted a phase II study aiming to assess the effectiveness of the FML regimen in 15 patients (pts) with measurable recurrent or metastatic colo-rectal carcinoma using two sequences of administration: regimen I: M 100/mg/m2 in D 5%/W over 30 min at time 0; F 600 mg/m2 iv push at 4 hrs and L 25 mg/m2 iv over 15 min at 24 hrs followed by 10 mg/m2 q 6 hrs po x 11 doses - q wk and regimen II which differed from the first only by the administration of F at 18 hrs instead of 4 hrs. All 5 pts on regimen II developed severe diarrhea, a sense of malaise and severe and persistent leukopenia at 7 days forcing a delay in the administration of the following course and leading to 2 dropouts. No partial remission (PR) was achieved; the 3 evaluable pts had a stabilization (DS) of their tumor growth lasting a mean of 9 wks. Instead 10 pts on Regimen I tolerated well the FML combination. They received an average of 5.2 courses. There were 8 PR (reduction of tumor size greater than 50%) for a mean of 18+ wks and 2 DS for a mean of 8.2 wks. All pts developed leukopenia with nadir at day 4 in 8 pts and at day 8 in two in whom the FML courses had to be administered q 2 wks. Seven pts had moderate diarrhea; 6 developed megaloblastic anemia. It is concluded that the FML appears to be active in colorectal carcinoma when F is administered 4 hrs after M while its administration after an 18 hr interval leads to unacceptable toxicity. (1 Ref)

42. HEMOLYTIC UREMIC SYNDROME DURING THERAPY WITH MITOMYCIN-C (MMC) PLUS 5-FLUOROURACIL (5-FU) (MEETING ABSTRACT)

Harden E, Lucas VS, Proia A, Silberman HR
Duke University Medical Center, Durham, NC, 27710
Proc Am Soc Clin Oncol; 1:C-360 1982

Reports of microangiopathic hemolytic anemia with renal failure in patients receiving MMC have been scanty, either citing the drug as causal or the carcinoma (often adeno) as responsible directly. Between 1977 and 1981, we have seen 8 patients develop a syndrome of malignant hypertension, fragmentation hemolysis, thrombocytopenia and renal failure during therapy with MMC plus iv 5-FU infusion. Total dose of MMC ranged from 45-199mgs and didn't seem to correlate with the etiology. Seven expired within 5 months of onset despite interruption of chemotherapy in all; a trial of corticosteroids in 3; and plasmapheresis in 1. Of two who had platelet antibody studies performed, both were positive and one had striking elevation of serum immune complexes. Although etiology isn't certain, during a randomized comparison of 5-FU, MMC, plus Vincristine vs 5-FU, semustine (Methyl CCNU) and Vincristine, for carcinoma of colon metastatic to liver, 5 of 26 patients in the MMC arm developed the syndrome in contrast to none of 28 in the Methyl CCNU group. Moreover, 4 of the 5 had objective evidence for regression of tumor at the time of onset of their hemolytic-uremic state. Of the 3 not in this study, 1 treated in an adjuvant setting for Duke's C colon cancer had no evidence of malignancy at autopsy while another with documented metastatic breast cancer during 2 years of chemotherapy and radiation did not develop the syndrome until after the chemotherapeutic regimen was revised to include MMC. (2 Refs)

43. REGIONAL INTRAARTERIAL (IA) MITOMYCIN C (MMC) INFUSION, ITS CLINICAL VALUE IN ADVANCED COLON RECTAL CANCER (MEETING ABSTRACT)

Tseng MH, Mittelman A
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Soc Clin Oncol; 1:C-358 1982

MMC when given intravenously caused severe cumulative myelosuppression, to improve its clinical application, MMC was used for regional IA infusion on patients (pts) who have unresectable colorectal cancer and failed all conventional chemotherapy. MMC 20 mg/M2 in 100 cc D5W was infused for 1 hr period through the arterial catheter into the tumor. When two organs were involved 1/2 of MMC was given respectively into each organ. The therapy repeated once every 6 wks. Chest x-ray and liver, bone, computerized transaxial tomographic scan were used for evaluation. Pretreatment complete blood count should be normal. Anemia was corrected by blood transfusion. Total of 35 pts have entered for infusion. These included 9 pelvic tumor, 4 pelvic and bone metastasis (met) 2 pelvic and lung met, 3 pelvic and liver met, 5 liver met, 8 involved lung and liver and 3 involved route of intestinal mesentery. Each pt has 1-5 infusions and received average MMC of 97 mgm. Four showed objective response and lived 14 months (m), 8 m, 7 m, and 6 m respectively. Eleven pts were stable for 3-9 m, 16 had no response and died within 2 m after progression, 4 lost to follow-up. Myelosuppression in these total 93 infusions showed 31 have Grade (G) 0, 15 had G-I, 33 had G-II, 10 showed G-III, and 5 have G-IV. One died from subdural hematoma. Three pts developed necrotic cellulitis of the buttock and required debridement and wound care. The other toxicity was mild. (no Refs)

44. INTERMITTENT HEPATIC ARTERY PERFUSIONS FOR SYMPTOMATIC METASTATIC COLON CARCINOMA (MEETING ABSTRACT)

Hatfield AK, Kammer BA, Daniey RA, Miller AG, Houston JG, Harder L
Carle Clinic Association, Urbana, IL, 61801
Proc Am Soc Clin Oncol; 1:C-395 1982

Twenty patients (pts) with colon carcinoma and symptomatic liver metastases received intermittent hepatic artery perfusions of 5-Fluorouracil (5-FU) and Mitomycin C given over a 5 day period. Only patients with serious liver involvement were chosen for therapy who had a limited life expectancy. Ten pts had previously received chemotherapy, 10 had not. Pts received Mitomycin C 0.2 mg/kg over 2 hours, followed by 5-FU 105 mg/kg over 120 hours. Pts initially received two perfusions 6 to 8 weeks apart. All pts were then followed with no maintenance chemotherapy. If symptoms returned pts were retreated until symptoms again disappeared. A total of 47 perfusions were given. Serious complications developed in less than 10% of perfusions. Overall, a 55% objective response rate was obtained. In previously untreated pts 90% responded, as compared to 28% in previously treated pts. Fifty percent of previously treated pts showed additional improvement, which did not meet standards for partial response used above. All responses were partial and no responses were complete. The median survival in all pts has been 14 months from the discovery of liver metastases and 8 months from the first liver perfusion. Fifty-five percent of our pts have developed symptomatic extraheptic sites of metastases which adversely influence a survival, but even in these pts the liver has been controlled as a site of disease in 54% until death from metastatic disease. This program has offered good palliation of pts symptoms and prolonged survival with a minimum of treatment. (no Refs)

45. INTRA-ARTERIAL CISPLATIN IN METASTATIC OR RECURRENT COLON CANCER (MEETING ABSTRACT)

Lehane DE, Zubler MA, Lane M, Smith FE
Baylor College of Medicine, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-365 1982

Chemotherapy for metastatic colon carcinoma has not been very effective in terms of response rate and/or survival. Fluorouracil has been the standard chemotherapy in this disease, and can result in 10 to 20% response rate and 2 to 3 month prolongation of survival. Cisplatin (CP) is not known to have therapeutic activity in colon cancer when administered intravenously. CP has increased activity administered intra-arterially. We report the results of treatment in 30 colon cancer patients, using intra-arterial CP infusions. CP was infused at 100 mg/m2. Vigorous hydration pre-and post-treatment and no diuretics were used. Pretreatment requirements included normal platelet, white blood counts and creatinine clearances (Ccr) greater than 70ml/min. Dose modifications were made for subsequent infusions. Of 30 patients, 1 is too early to evaluate for response, 3 complete responses, 18 partial responses and 8 no responses were observed. There was frequent relief of sacral plexus pain (6/7). The mean and median response durations are 8.3 and 7+ months, and mean and median survival are 9.7 and 11+months. Toxicity was not different than anticipated for CP. Twelve patients had a 25% or greater increase in serum creatinine, only 2 had a 2-fold increase in serum creatinine, and no patients had a serum creatine greater than 2.5. Low grade temporary fever was seen in 4 patients and hyponatremia was found in 2 patients. (no Refs)

46. ADJUVANT THERAPY BY INTRA-ARTERIAL INFUSION FOR ADENOCARCINOMA OF THE COLON (DUKES' C) PROGRESS REPORT (MEETING ABSTRACT)

Campos LT, Sinkovics JG, Fisher RG, Copeland OP, Peddie G, Weaver RM, Murphy JF, Khera H, Max E
No affiliation given
Proc Am Soc Clin Oncol; 1:C-273 1982

Twenty-five patients (pts) who underwent curative surgery for adenocarcinoma of the colon between May 1976 and December 1977 received adjuvant chemotherapy by intra-arterial infusion (IAI) via transfemoral catheterization of the celiac axis with vincristine 2mg followed by mitomycin C 10mg/M2 on day 1 and 5-FU (5-fluorouracil) 5,000mg/M2 by continuous infusion. CCNU (lomustine) 100mg/M2 was given po on day 2. Eight courses were administered at six weeks intervals. In addition, pts were randomized to receive BCG by scarification for 2 years. At a median follow-up of 56 months three pts (12%) have recurred at 18, 19 and 37 months after surgery. The first two pts died, neither one had hepatic metastases (autopsy-proven), the third one had a solitary nodule in the lung, resected 6 months after discovery. She is free of disease (FOD). Toxicity was acceptable. Between February 1978 and December 1980, 32 pts received adjuvant chemotherapy by IAI with the above program but CCNU and BCG were omitted. At a median follow-up of 36 months all pts are free of tumor. One pt died of pulmonary edema 6 months after finishing chemotherapy (FOD autopsy-proven) one pt develped perforated gastric ulcer 3 months after her last course of chemotherapy. Complications and toxicity were reported before. Twelve pts with Dukes' B carcinoma of the colon received 4 courses of this regimen. Median follow-up 14 months. All pts are FOD. (2 Refs)

47. TRANSAXILLARY HEPATIC ARTERY CHEMOTHERAPY USING AN IMPLANTED DRUG PUMP (MEETING ABSTRACT)

Cohen AM, Wood WC, Greenfield A
Massachusetts General Hospital, Boston, MA, 02114
Proc Am Soc Clin Oncol; 1:C-348 1982

The objective of this study was to evaluate the feasibility of integrating an implantable, refillable drug infusion pump with transaxillary angiographic hepatic arterial catheterization. The implantation is performed under local anaesthesia in the radiology suite. A 2-3 cm incision in the left upper arm is made through skin and subcutaneous tissue. Through an axillary artery puncture, a 5.3F polyethylene catheter is fluoroscopically placed into the hepatic artery. To minimize gastroduodenitis, the gastroduodenal artery is occluded with a Gianturco coil and Gelfoam. The Model 400 Infusaid pump is implanted in the upper chest and attached subcutaneously to the angiography catheter using a friction connector. Patients are discharged 2-3 days later. Over a 2 year period, 20 such implants have been performed. Fluorodeoxyuridine (FUdR) has been used by continuous infusion; Mitomycin-C (MMC) and carmustine (BCNU) by intermittent intra-arterial infusion. The pump/catheter system has been left in place for as long as 18 months. Partial responses in the colorectal cases are as follows: FUdR 4/9, MMC 2/3, FUdR + MMC 1/1, FUdR + MMC + BCNU 3/3. No arm vascular complications, hepatic arterial occlusions, peripheral emboli, pump malfunctions, or catheter occlusions took place over a total experience of 3,210 patient days. Three catheter migrations occurred requiring repositioning in 2, and 3 cracked catheters required replacement. This innovative approach offers a comfortable, convenient method for long-term ambulatory hepatic arterial chemotherapy obviating both laparotomy and extra-corporeal pumps. (no Refs)

48. CONTINUOUS HEPATIC ARTERY INFUSIONS OF FUDR WITH A TOTALLY IMPLANTED INFUSION PUMP (MEETING ABSTRACT)

Weiss GR, Garnick MB, Schade D, Osteen RT, Kaplan W, Steele GD, Wilson RW, Sack MJ, Steckel SD, Mayer RJ, Frei E
Sidney Farber Cancer Institute, Boston, MA, 02115
Proc Am Soc Clin Oncol; 1:C-361 1982

Clinical data confirm that hepatic artery infusion of chemotherapy has a definite role in the treatment of selected patients with primary and metastatic carcinoma of the liver. We have treated 13 patients (pts) with colorectal carcinoma with long term, continuous hepatic artery infusion (HAI) Fluorodeoxyuridine (FUdR) using the Infusaid pump. The pump is implanted subcutaneously in the abdominal wall and connects to a surgically placed silastic catheter in the gastroduodenal or common hepatic artery. FUdR is given for two weeks (w) followed by a 1-2 w 'break' period. Starting dose is 0.2 mg/kg/day and may be escalated by 0.1 mg/kg increments depending upon pt tolerance. Mean duration of treatment had been 7.7 w. Toxicity of FUdR infusion included elevated alkaline phosphatase and SGOT in 7 pts, jaundice in 3 pts, epigastric and central chest pain in 4 pts, and diarrhea in 2 pts. All pts experience mild nausea and/or mild anorexia at some time during treatment. Of 8 pts evaluable for response of hepatic disease to therapy, two partial responses (PR), one minor response, 4 stable disease and one progressive disease were observed for an objective response rate of 25%. One pt with a PR was rendered disease-free by resection of the residual hepatic mass. Three pts whose hepatic disease remained stable developed extrahepatic disease. (no Refs)

49. LEVAMISOLE AND 5-FLUOROURACIL IN METASTATIC COLORECTAL CARCINOMA (MEETING ABSTRACT)

Davis TE, Borden EC, Wolberg WH, Crowley JJ
University of Wisconsin Clinical Cancer Center, Madison, WI, 53792
Proc Am Soc Clin Oncol; 1:C-396 1982

In animal tumor models, the most consistent effects of levamisole (lev), a synthetic phenylimidazothiazole, have been observed when used in combination with chemotherapy. We therefore initiated a trial in which patients with metastatic colorectal carcinoma, who were of good performance status (PS) and had not received prior radiotherapy or chemotherapy were prospectively randomized to cyclic loading courses every 6 weeks of 5-fluorouracil (5-FU) (12 mg/kg intravenously daily x 5; then 6 mg/kg on alternate days to toxicity) or 5 FU and lev (2.5 mg/kg orally on days 28, 29, 35 and 36 of each cycle). A total of 82 fully eligible and evaluable patients were entered on this trial. The only patient or disease characteristics to significantly influence survival were PS and presence of measureable disease. Patients who received 5 FU and lev survived longer than those who received 5 FU alone. Adjustments according to a Cox regression model for the influence of PS or measureable disease did not influence this treatment difference. There also were no significant differences in the severity of toxicities between the two treatments (Fisher's exact test). (no Refs)

50. A PHASE I STUDY OF RECOMBINANT DNA PRODUCED LEUKOCYTE INTERFERON BY AN INTERMITTENT SCHEDULE (MEETING ABSTRACT)

Quesada JR, Gutterman JU, Fein S
M. D. Anderson Hospital and Tumor Institute, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-140 1982

A clinical study was conducted to determine the human tolerance and pharmacokinetics of intermittent doses of recombinant DNA produced pure leukocyte interferon (IFLrA) in cancer patients (pts). Twenty-five adults pts with advanced cancer (9 colon, 7 breast, 1 renal, 1 ovarian carcinomas; 6 lymphomas and 1 malignant fibrohistiocytoma) received IFLrA intramuscularly twice per week in groups of sequential escalating doses from 9 to 68 million units (MU). Fifteen pts are evaluable for pharmacological analysis and toxicity. Median maximum serum concentrations measured by bioassay were 107, 120 and 250 u/ml 8 hrs after a dose of 9, 18 and 36 MU respectively. Median serum concentration at 24 hrs for each of these doses were 10, 20 and 150 u/ml indicating slower clearance at higher doses. Pts received IFLrA from 3 to 12 weeks. The clinical side effects consisted of fever, chills and myalgias following almost all doses. These symptoms resolved spontaneously within 24 hrs. Headaches and gastrointestinal symptoms occurred frequently. Fatigue and anorexia persisted in all pts while on treatment. Dose reduction was indicated in one pt at 18 MU. Hematological toxicity consisted of reversible leukopenia and neutropenia. Median nadir was 2.4, 2.6 and 2.7x10(3) leukocytes mm-3 and 1.3, 1.7 and 1.3x10(3) neutrophils mm-3 at 9, 18 and 36 MU respectively. Hemoglobin decreased in 85% of the pts. No major adverse effects were seen in blood chemistries. Objective antitumor effect has been seen in 3 pts with lymphoma and 1 pt with breast cancer so far. (no Refs)

51. A PHASE I TRIAL OF TWICE DAILY RECOMBINANT HUMAN LEUKOCYTE A INTERFERON (IFL-RA) IN CANCER PATIENTS (MEETING ABSTRACT)

Leavitt RD, Duffey PL, Wiernik PH, Fein S, Sherwin S, Scogna D, Oldham R
Baltimore Cancer Research Center, University of Maryland, Baltimore, MD, 21201
Proc Am Soc Clin Oncol; 1:C-162 1982

A phase I study of IFL-rA was performed in patients (pt) with advanced cancers and hematologic malignancies. At least 5 pt were entered at each dose level of 1,3,9,18,36,54 and 72 x 10(6) U/d and received IFL-rA intramuscularly twice daily for 28 days (d). Pharmacokinetics were determined. Results of immunologic monitoring will be reported separately. Constitutional symptoms are frequent. A 'flu-like' syndrome occurs early with chills, fever, headache, myalgias, and lethargy. Rapid tolerance to fever develops, but low grade fever may persist. Mild to moderate anorexia, nausea, vomiting, and diarrhea may occur. Fatigue, frequently progressive, is potentially dose limiting at 72 x 10(6) U/d. Transient paresthesias or numbness occurred in 2 pt. Dose related neutropenia and hepatotoxicity, unacceptably severe at 72 x 10(6) U/d, were tolerable at 54 x 10(6) U/d. Partial recovery from neutropenia often occurs while on treatment. Recovery from toxicity begins in days of stopping IFL-rA and was complete in all pt. Objective responses were seen in 7 pt (2 myeloma, plasmacytoma, nodular lymphoma, renal cell, adenocarcinoma of prostate and colon) receiving 36 or 54 x 10(6) U/d. Two of 3 measurable lesions completely regressed in the pt with renal cell carcinoma, who continued 54 x 10(6) U, 3x/wk. Phase II solid tumor studies are planned with 54 x 10(6) U/d given bid x28d. (no Refs)

52. PHASE I CLINICAL TRIAL OF INFUSION INTO CANCER PATIENTS OF AUTOLOGOUS LYMPHOCYTES ACTIVATED IN VITRO WITH LECTINS (MEETING ABSTRACT)

Mazumder A, Grimm EA, Eberlein T, Rosenberg SA
Surgery Branch, National Cancer Institute, Bethesda, MD, 20205
Proc Am Soc Clin Oncol; 1:C-158 1982

We have previously demonstrated that peripheral blood lymphocytes (PBL) of cancer patients can be activated by lectins to lyse fresh autologous tumor cells (FATC) but not normal cells in vitro. A clinical protocol has been instituted in cancer patients who had failed all other therapies to determine the toxicity and effects in vivo of the infusion of large numbers of autologous activated PBL. Eight patients have thus far been entered into the protocol, 5 sarcomas, 1 melanoma, 2 colorectal cancer. Up to 1.7x10(11) PBL were obtained from 9 to 14 successive leukaphereses and incubated in vitro in medium containing phytohemagglutinin (PHA) and human AB serum for 2 days and then reinfused following the next leukapheresis. Toxicity included fever and chills in 8/8 patients, headaches in 5/8, transient nausea and vomiting in 3/8 and a mean decrease of 30% in pulmonary diffusion capacity that reversed within 24 hours in 6/6 patients tested. Six of eight patients required 1 unit of RBC tranfusion. In 6/6 patients, highly activated PBL were found in the circulation by the sixth leukapheresis. The background incorporation of 3H-Tdr (thymidine) into PBL increased from 3 to 7 fold with successive leukaphereses and could be enhanced in vitro by the addition of lectin free T cell growth factor. PBL lytic for FATC also increased from 2% initially to 27% on successive fresh PBL collections in 6/6 tested. Thus far no significant clinical effects have been seen. Thus, it appears that large numbers of autologous PHA activated PBL can be safely obtained and infused into humans, achieving an increase in the number of circulating activated cells. (no Refs)

53. SWOG TRIAL OF TAMOXIFEN IN PATIENTS WITH ADVANCED COLORECTAL ADENOCARCINOMA (MEETING ABSTRACT)

Panettiere FJ, Chen TT
No affiliation given
Proc Am Soc Clin Oncol; 1:C-364 1982

Reports that approximately 25% of large bowel adenocarcinomas in men and in women contain estrogen-binding proteins led to SWOG 7910, a study testing the antiestrogen drug, Tamoxifen, in the management of such tumors. For eligibility it was required that the tumor be measured in at least two different dimensions. Tumor assay for estrogen receptor was encouraged, but not required. Prior chemotherapy exposure made one ineligible unless: (1) it were given as an adjuvant no less than 6 months previously, or (2) the patient's tumor tissue had been submitted for estrogen receptor assay. Between June 1979 and September 1980, 54 eligible patients were entered. Three had had prior chemotherapy exposure (and did not respond to Tamoxifen). Of the 51 without prior chemotherapy exposure, 4 (8%) had partial regressions by standard criteria. The durations of these regressions were 40, 78, 107, and 290 days. An additional 8 patients (16%) had stable disease lasting at least 90 days. The median duration of survival of the 51 who had Tamoxifen as initial therapy was 29 weeks. No patient receiving Tamoxifen experienced leukopenia or thrombocytopenia. Twenty-nine percent experienced transient nausea only; 21% vomited and in one this toxicity led to discontinuance of therapy. Other reported adverse effects were thrombophlebitis, headaches, and hallucinations which may have resulted from water retention. (no Refs)

54. CLINICAL PHASE I STUDY OF A NEW RETINOID (RO 13-6298) (MEETING ABSTRACT)

Hartmann D, Hofmann V, Hindermann W, Isler A, Weber E, Obrecht J, Honegger H, Martz G, Germano G, Bollag W
University of Basle (Kantonsspital), CH-4031 Basle, Switzerland
Proc Am Soc Clin Oncol; 1:C-595 1982

Ro 13-6298 is a new retinoid with a favorable therapeutic index and documented anticancer activity in animals. In this study, the agent was given PO either once weekly (group 1) or daily for 28 days (group 2). Group 1 (9 males, 2 females, median age 63 y) comprised 5 lung cancers, 4 melanomas, 1 gastric cancer, 1 undifferentiated cancer. The following doses were evaluated: 5.0 mcg/kg/week, 7.5 mcg/kg/week, and 10.0 mcg/kg/week. Skin toxicity (scaling, desquamation, dryness of mucous membranes, cheilitis and erythema) occurred in 10 of 11 patients, being severe in 1 patient (loss of fingernails). Group 2 (9 males, 3 females, median age 62 y) comprised 3 lung cancers, 2 melanomas and 1 cancer of the bladder, thyroid gland, penis, kidney, cervix, colon and skin. The retinoid was given at doses of 1.0, 1.5, and 2.0 mcg/kg/day. Skin toxicity occurred in 10/12 patients, being severe in 1. Mild side effects other than mentioned in both groups consisted of dizziness, headache, loss of appetite, constipation, hair-loss and pain at the sites of metastases. Response to treatment in group 1 was no change (NC) in 5, and progression (PD) in 6 patients, in group 2 all patients showed stable disease (NC) during the treatment. (no Refs)

55. CRYOTHERAPY OF CANCER OF THE COLON.

Scholzel E, Langer S
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Helv Chir Acta; 48(6):867-872 1982

Cryotherapy (CT) was employed in treatment of cancer of the colon in 184 patients. Criteria for CT as sole therapy were advanced age combined with serious secondary disease, advanced tumor growth with distant metastases, and refusal of surgery. CT was employed in combination with other therapy in 33 cases. CT involved freezing of tumor tissue to-185 C within 1-2 min, maintaining the temperature for 1-2 min, and slow thawing. Overlapping treatments were performed at 2-4-wk intervals, begun 4-8 wk after removal of tumor stenoses. Complete tumor destruction was achieved in 30 patients, including 20 with Stage A or B tumors. Tumors recurred in five cases; in three of these cases the recurrence was destroyed with CT. In cases in which tumor destruction was not complete, tumor symptoms (bleeding, mucous discharge, tenesmus, ileus, and incontinence) were relieved. Two thirds of the patients were alive after 2 yr. Five patients were alive after 5 yr. Eleven patients died of carcinoma or related effects. Among patients with inoperable tumors survival time was 50% longer than with other palliative measures. CT was performed 3-4x prior to surgery in 33 cases. In 6/33 cases no tumor tissue could be found in surgical specimens. Advantages of CT include minimal burden to the patient, use on an outpatient basis without anesthesia, and avoidance of colostomy in many cases. (8 Refs) (In GER)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

56. CARCINOMA OF THE COLON AND RECTUM IN YOUNG ADULTS.

Hsu YH, Guzman LG
298 Todt Hill Road, Staten Island, NY, 10314
Am J Proctol Gastroenterol Colon Rectal; 33(4):7-8,10-12 1982

Eighteen cases of colorectal cancer diagnosed in patients (13 men, 5 women) 20-40 yr old, obtained from the retrospective study of 381 carcinomas of the colon and rectum, are reviewed and analyzed. Incidence of tumors in the 18 patients increased with age. Presenting symptoms included rectal bleeding (11/18 patients), abdominal pain (8/18), wt loss (4/18), and diarrhea (4/18). Duration of symptoms is reported: 0-1 mo, 3/18 patients; 1-3 mo, 7/18; 3-6 mo, 6/18; and 6-12 mo, 1/18; one patient was diagnosed at autopsy. Of the 18 tumors, 2 were fibrosarcomas, 2 were mucinous adenocarcinomas, and 14 were adenocarcinomas. Two patients had ulcerative colitis and one had familial polyposis. Twelve of the tumors were located in the left colon or rectum, 6 in the right colon, and 1 in the transverse colon. Curative surgery was performed: hemicolectomy or anterior sigmoid colon resection (12 patients), abdominoperineal resection (2), pelvic exenteration (1), total colectomy (1), and subtotal colectomy (1). Depth of invasion and presence of lymph node metastases were important prognostic factors. All 6/16 patients with adenocarcinoma who died within 4 yr of diagnosis had tumors involving the serosa layer and 4/6 had lymph node involvement. Ten patients were alive with a follow-up of 1-12 yr. The development of colorectal cancer in young adults is discussed. (34 Refs)

57. AGE DISTRIBUTION OF RIGHT- AND LEFT-SIDED COLORECTAL CANCERS.

Slater G, Papatestas AE, Tartter PI, Mulvihill M, Aufses AH
Dept. Surgery, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY, 10029
Am J Gastroenterol; 77(2):63-66 1982

The age distributions in different anatomic areas of the colorectum were compared in 410 patients. The av age for patients with right-sided cancers (71.3 yr) was significantly higher than that for patients with left-sided cancers (67.5 yr). In addition, there was a significantly higher percentage of patients over the age of 70 (mean age of the whole group) in the right colon group as compared with the left colon group. It was concluded that the older age distribution of right-sided cancers might be explained by the delayed effect of an environmental carcinogen in a population with a longer life expectancy. (Author abstract) (27 Refs)

58. DIAGNOSIS AND SURVIVAL IN CARCINOMA OF THE LARGE BOWEL.

Jolly KD, Scott JP, MacKinnon MJ, Clarke AM
(c/o Clarke) Dept. Surgery, Univ. Otago Medical Sch., P.O. Box 913, Dunedin, New Zealand
Aust NZ J Surg; 52(1):12-16 1982

Diagnostic delay was measured in 455 consecutive patients who had large bowel cancer and it was found to be less pronounced than in a previous study in the same hospitals. However overall corrected 5 year survival remained the same. The duration of symptoms was not correlated with the stage of the disease, nor with 5 year survival. The pattern of disease resembled other Western series, with an overall corrected 5 year survival rate of 33.2%. Prognosis was significantly better in women and worse in patients with an elevated ESR on presentation. Intestinal obstruction due to carcinoma did not adversely affect prognosis. (Author abstract) (12 Refs)

59. CROHN'S DISEASE ASSOCIATED WITH CARCINOMA OF THE COLON.

Reddy P, Hyland J, Clery AP
(c/o Clery), Richmond Hosp., Dublin 7, Ireland
Ir Med J; 75(3):84,86 1982

Three cases of coincidental Crohn's disease associated with adenocarcinoma of the colon are reported. In two of the cases, initial presentation was for symptoms of Crohn's disease. In the third case, diagnosis of Crohn's disease was incidental to colon carcinoma. The present findings represent an incidence of 10% of cases of Crohn's colitis observed of a 10-yr period. Carcinoma of the colon may be a complication of long-standing Crohn's disease. (17 Refs)

60. LARGE BOWEL CANCER: AN OVERVIEW.

Higgins GA
Veterans Admin. Medical Center, 50 Irving St., NW, Washington, DC, 20422
Aust NZ J Surg; 52(1):5-12 1982

Cancer of the large bowel is a problem of international scope but with wide national incidence variations possibly related to climatic factors. Neither etiologic studies nor improved methods of early detection have thus far had an impact on national death rates. Surgical treatment, while comparatively effective, does not promise a significant increase in survival data, and thus far, adjuvant therapies have failed to fulfill early enthusiastic expectations. Nevertheless, continued research pursuit of the nature of the neoplastic process, development and application of improved diagnostic and screening methods, and synthesis of better combined modality therapy, will result in substantial improvements in therapeutic results. (Author abstract) (38 Refs)

61. ADENOCARCINOMA OF THE ASCENDING COLON SHOWING LONGITUDINAL GROWTH AND ASSOCIATED WITH METACHRONOUS ENDOMETRIAL CARCINOMA: REPORT OF A CASE.

Takami M, Kimura M, Hanada M, Takeuchi N, Asoh R, Maeda T, Shimizu H, Yoshii M
Dept. Surgery, Toyonaka Municipal Hosp., Toyonaka, Japan
I To Cho; 17(3):331-336 1982

Barium enema study showed a large, longitudinally elevated lesion extending from the terminal ileum to the proximal two-thirds of the ascending colon in a 50-yr-old woman with complaints of right lower abdominal pain. Based on the roentgenographic and colon fiberscopic findings, the tumor was resected; examination showed the tumor to be confined within the intestinal wall and consisting of moderately-differentiated and mucinous adenocarcinomas. Two yr postoperatively, the patient developed primary endometrial carcinoma. The patient's brother had surgery for multiple colon and multiple gastric cancers, the patient's sister died from gastric cancer, and the patient's father died of colon cancer. (15 Refs) (In JPN)

62. RECTAL MALIGNANT LYMPHOMA IN CHRONIC ULCERATIVE COLITIS.

Bartolo D, Goepel JR, Parsons MA
Dept. Surgery, Royal Hallamshire Hosp., Sheffield, England
Gut; 23(2):164-168 1982

Carcinoma of the colon as a complication of ulcerative colitis is relatively common, whereas malignant lymphoma is apparently rare; there are approximately 20 recorded cases. We report a case of follicular lymphoma of the rectum in a 73 yr old woman with a 21 yr history of ulcerative colitis. In view of the possible immune basis of ulcerative colitis, it is important to report and accurately classify cases of lymphoma arising in association with it. (Author abstract) (26 Refs)

63. COLIC CARCINOMA AND BASAL CELL EPITHELIOMA ELEVEN YEARS AFTER KAPOSI SARCOMA WITH SPLENIC AND CUTANEOUS INVOLVEMENT.

de Plunkett TL, Pieron R, Dreyfus F, Meyniel D
Service de Medecine Interne, Hopital Tenon, 4, rue de la Chine, 75020 Paris, France
Sem Hop Paris; 58(17):1027-1030 1982

A case of Kaposi sarcoma (KS) with cutaneous and splenic involvement is reported. Carcinoma of the left colon and basal cell epithelioma arose 11 years after KS. Genetic, viral, and immunologic factors which may promote initiation and development of Kaposi sarcoma are reviewed. The responsibility of immunodeficiency, whether resulting from therapy or from other causes, in carcinogenesis is discussed. Prolonged survival may be seen after KS. Another primary malignant disease (lymphoma or solid tumor) may arise. The authors suggest that the risk of immunologic disorders, occurring spontaneously or induced by therapy, should be considered specifically for each patient with KS. (Author abstract) (14 Refs) (In FRE)

64. CARCINOMA ARISING IN AN ILEOSTOMY STOMA. AN UNUSUAL COMPLICATION OF ADENOMATOUS POLYPOSIS COLI.

Roth JA, Logio T
Dept. Pathology, Overlook Hosp., Summit, NJ, 07901
Cancer; 49(10):2180-2184 1982

A patient with adenomatous polyposis coli (APC) without extraintestinal lesions is presented. The clinical course was complicated by rectal adenocarcinoma following subtotal colectomy. A primary adenocarcinoma arising in a villous adenoma within the ileostomy stoma developed 7 yr later. The varied pathology of gastric and small intestinal involvement in APC/Gardner's syndrome is reviewed. Greater awareness of these lesions has implications for further management. (Author abstract) (33 Refs)

65. TAMOXIFEN INDUCED REMISSION OF DESMOID TUMORS (MEETING ABSTRACT)

Kinzbrunner B, Ritter S, Rosenthal CJ
Downstate Medical Center, Brooklyn, NY, 11203
Proc Am Soc Clin Oncol; 1:C-699 1982

Experimental studies have suggested that estrogens may stimulate desmoid growth. We now report the apparent response to anti-estrogen therapy of recurrent desmoids in a case of Gardner's syndrome. A 29 yr. female was hospitalized for a 6 mos history of anorexia and 20 lbs weight loss and the recurrence after extirpation from her back during the last three years, of two large desmoid tumors weighing 4 and 35 lbs. Her physical examination was significant for her emaciation and for the presence of several subcutaneous masses; in the mid lumbar region (12 x 5 cm), under the right scapula (8 x 8), and along the left lateral border of the scar of her back (4 small nodules). The biopsy of one of them confirmed the diagnosis of desmoid. Further evaluation revealed multiple polyposis coli, adenocarcinoma of the colon sigmoid with liver metastases and multiple osteomas of her skull and pelvis leading to the diagnosis of Gardner's Syndrome. Due to the development of intestinal obstruction the patient underwent a palliative diverting procedure. During the recuperative period because of severe pain from the desmoids of her back, she was started on Tamoxifen 80 mg per day in 4 divided doses. Within 3-4 days her paid was relieved. After 2 wks of therapy a significant reduction of the desmoid masses was noted: the small scar nodules disappeared, the ovoid lumbar mass decreased by 80% while the scapular round mass was reduced by 50%. Unfortunately, patient expired after developing sepsis and hypoglycemia. (no Refs)

66. AMYLOIDOSIS MASQUERADING AS INFLAMMATORY BOWEL DISEASE WITH A MASS LESION SIMULATING A MALIGNANCY.

Johnson DH, Guthrie TH, Tedesco FJ, Griffin JW, Anthony HF
Div. Oncology, Dept. Medicine, Vanderbilt Univ., Nashville, TN, 37232
Am J Gastroenterol; 77(3):141-145 1982

Our patient, who was known to have multiple myeloma, presented with wt loss, rectal bleeding, and a barium enema study suggestive of a colitis with a mass lesion. Colonoscopy with biopsy revealed the mass to be large mucosal folds infiltrated with amyloidosis. Amyloidosis has been reported to mimic malignancy, mainly by tumorous deposits in the stomach and less commonly in the small and large bowels. Gastrointestinal surgery in patients with amyloidosis potentially may have undesirable consequences due to failure of anastomotic suture lines and subsequent sepsis. The knowledge that amyloidosis may be associated with multiple myeloma and an appreciation of the wide range of gastrointestinal roentgenographic findings in patients with amyloidosis should prompt the clinician to obtain endoscopic and biopsy evaluation of these patients. (Author abstract) (27 Refs)

67. RAPID ASSAY FOR EVALUATING THE CHEMOSENSITIVITY OF HUMAN TUMORS IN SOFT AGAR CULTURE.

Tanigawa N, Kern DH, Hikasa Y, Morton DL
Div. Surgical Oncology, UCLA Sch. Medicine, Ninth Floor, Factor Building, Los Angeles, CA, 90024
Cancer Res; 42(6):2159-2164 1982

Assays that measure [3H]thymidine incorporation by cells plated in soft agar were investigated to identify a rapid method for assessing chemosensitivity of tumor cells. Six established cell lines (5 melanomas and 1 colon carcinoma) and cells prepared from 23 primary or metastatic tumors (10 melanomas, 5 colon adenocarcinomas, 3 lung carcinomas, 2 ovarian adenocarcinomas, 1 breast adenocarcinoma, and 1 leiomyosarcoma) were tested. The end point of tritium incorporation was measured by autoradiographs (labeling index) and scintillation counting (cpm) after 24-hr labeling. When results were compared, there was a strong correlation between the two assays (p less than 0.0001). However, the scintillation counting assay had major advantages: (a) counting incorporated radioisotope was technically easier than the autoradiographic method; (b) the DNA synthesis rate of the whole tumor cell population could be evaluated, not that of tumor colony-forming cells alone; and (c) the sampling error was minimized since the procedure was done automatically. There was significant association between cpm values 48 to 72 hr after plating and the number of colonies formed at 2 to 4 wk in control dishes (p less than 0.001). Eighteen of 23 surgical specimens (78%) and all four cell lines were evaluable. Chemosensitivity was assessed after 48 hr of plating with alkylating agents, antibiotics, and Vinca alkaloids and after 72 hr with 5-fluorouracil and methotrexate. Results suggested that an 80% or greater reduction of [3H]thymidine incorporation was correlated with a 75% or greater decrease in colony growth (p less than 0.0001). Thus, this scintillation assay accurately predicted drug-tumor interactions within 5 days that resulted in a 75% or greater decrease in colonies. (Author abstract) (28 Refs)

68. THE SUBRENAL CAPSULE ASSAY AS A SENSITIVITY TEST FOR DETERMINATION OF THE RESPONSE OF INDIVIDUAL TUMORS TO SPECIFIC CANCER CHEMOTHERAPEUTIC AGENTS (MEETING ABSTRACT)

Griswold DP, Dykes DJ, Corbett TH, Schabel FM
Southern Research Institute, Birmingham, AL, 35255
Proc Am Assoc Cancer Res; 23:873 1982

Bogden et al have recently reported on the development of the subrenal capsule (SRC) assay of human tumors in mice. Their purpose was twofold: (1) the evaluation of anticancer activity of new agents prior to clinical testing and (2) selection from clinically available chemotherapeutic agents those most likely to have activity against an individual patient's cancer. We began an attempt to validate the SRC assay using a variety of mouse colon tumors for which the response of each tumor line to various chemotherapeutic agents was already known. We used 10 mouse colon tumor lines that were developed, 4 of which have been previusly described by Corbett et al. Nine chemotherapeutic agents were selected based on historical evidence of antitumor activity that ranged from marked to none. The procedures of Bogden et al were basically followed with only necessary exceptions. To provide internal controls, mice with subcutaneous (SC) implants were treated in the same manner as those with SRC implants. Since mouse tumors were used, mice allogeneic for the particular tumor were used for SRC implants, whereas syngeneic mice were used for SC implant controls. Preliminary results from 4 of the tumor lines show a positive correlation in antitumor activity or inactivity for SRC or SC tumors in 22/27 or 26/27 trials depending on the level of activity used as the cut off. (2 Refs)

69. ACTIVITY OF DRUGS AGAINST HUMAN TUMORS AS DETERMINED BY THE 6-DAY SUBRENAL CAPSULE (SRC) ASSAY (MEETING ABSTRACT)

Reich SD, Griffin TW, Antonelli DM, Costanza ME, Bogden AE
Division of Clinical Pharmacology, University of Massachusets Medical School, Worcester, MA, 01605
Proc Am Assoc Cancer Res; 23:875 1982

For the purpose of screening new anticancer drugs, it is important to detect and confirm activity against a heterogeneous tumor population in a cost effective manner. Although the SRC Assay was originally designed to utilize transplantation established human tumors for screening new anticancer agents in an 11-day assay using athymic mice, it has been modified to employ normal mice, tumor tissue obtained from patients by surgical excision, and a 6-day time frame. Most of the drugs employed in the assay were chosen on the basis of known clinical activity against a particular tumor type. The number of tumors (assays) required to find and confirm activity was determined for the most active agents (in the assay). Drugs are listed in descending order of activity. breast tumor: L-Phenylalanine mustard (L-PAM) (3), Cyclophosphamide (CTX)(3), 5-Fluorouracil (5-FU)(6), cervical tumor: CTX(4), Bleomycin (BLEO)(4), Methotrexate (MTX)(8), Adriamycin (ADR)(2), colon tumor: 5-FU(3), CTX(3), ADR(7), endometrial tumor: 5-FU(6), MTX(4), Vincristine (VCR) (4), CTX(6), kidney tumor: 5-FU(5), CTX(2), ADR(3), lung (all types): CTX(2), MTX(2), Procarbazine(14), lymphoma: CTX(3), VCR(3), MTX(2), melanoma: Dacarbazine (DTIC)(3), Carmustine (BCNU)(7), L-PAM(4), ADR(5), ovarian: 5-FU(2), CTX(2), L-PAM(2), sarcoma: MTX(5), DTIC(7), 5-FU(3), CTX(6), Mitoxantrone, a new agent, was found to be active in breast and gastric carcinoma and lymphoma within 4 tumor specimens of each type. These results suggest that drugs of high clinical activity directed against specific tumors can be detected by testing only a few surgical, tumor specimens without the expense of facilities for athymic mice and serial, tumor transplantation. (no Refs)

70. EFFECTS OF LOW-OXYGEN CONCENTRATION ON PROLIFERATION OF HUMAN TUMOR CELLS IN SOFT AGAR (MEETING ABSTRACT)

Sridhar KS, Plasse T, Ohnuma T, Shapiro M, Kirshner PA, Holland JF
Mt. Sinai School of Medicine, New York, NY, 10029
Proc Am Soc Clin Oncol; 1:C-46 1982

In vitro chemotherapy sensitivity of direct human tumor explants on semisolid agar has shown some correlation with in vivo responses, but the technique has been limited by low cloning efficiency (CE). Only 25% of the specimens grown in culture formed greater than 30 colonies in control plates and had enough cells in tumor specimens to enable at least one in vitro drug-sensitivity assay to be performed. Cells were routinely incubated with 5% CO2, 95% room air. Twenty-four consecutive fresh tumor specimens--9 ovarian epithelial, 3 ovarian germ cell, 4 colon, 3 lung, 1 each of breast, pancreas and endometrial carcinoma, 1 carcinoid, and 1 mesothelioma--were plated at a concentration of 2x10(5) nucleated cells (ovarian) or 5 x10(5) (other cancers) and incubated with (A) 5% CO2, 5% O2, 90% N2 or (B) 5% CO2, 95% room air. Eighteen solid tumor samples were minced and disaggregated in 0.25% collagenase-0.02% DNAse prior to plating. Twenty-two of the 24 samples showed an increase in CE in (A) compared to (B). The CE of all samples in (A) increased 2-fold from a mean of 0.039% to 0.078%. Of the 9 ovarian epithelial cancers, 7 had more than 30 colonies per plate under either (A) or (B). The CE of the 7 samples in (A) had a mean 5.6-fold increase over (B); 3 had 9-to 12-fold increases. A mean increase in CE of lung carcinoma was 3-fold; of colon, 1.35-fold; of miscellaneous tumors, 2.7-fold. In (A) 20/24 grew more than 30 colonies per plate; in (B) 17/24 grew more than 30. These data indicate that 5% O2, 5% CO2, 90% N2 is a better gas phase for colony formation for certain human carcinomas, and increases the ability to carry out drug assays. (no Refs)

71. NMR RELAXATION TIMES OF WATER PROTONS IN HUMAN COLON CANCER CELL LINES AND CLONES.

Beall PT, Hazlewood CF, Rutzky LD
(c/o Rutzky) Dept. Surgery, Biochemistry and Molecular Biology, Univ. Texas Medical Sch., Houston, TX, 77030
Cancer Biochem Biophys; 6(1):7-12 1982

Established lines of human colon cancer cells from several sources (LS180, LS174T, HT29, SW480, SW1345) had water proton nuclear magnetic resonance (NMR) spin-lattice relaxation times (T1) of 460 +-45 msec to 982 +-9 msec and spin-spin relaxation times (T2) of 83 +-6 msec to 176 +-6 msec. Two clones derived from single cells of line LS174T were similar in T1 and T2 to the parent line. Differences among the cell lines were not totally a function of cellular hydration. Normal adult and fetal human primary colon cells were wetter and had higher T1 and T2 values than established cell lines. Relaxation times in this study substantiate variations seen for human colon tumors in earlier studies. Established cell lines maintained water relaxation times similar to tumor tissue values. Along with other morphological and biochemical criteria, the relaxation times suggest that these established human colon cancer cell lines may serve as a good experimental model for the study of human colon cancer. (Author abstract) (44 Refs)

72. DIFFERENTIAL EXPRESSION OF TUMOR ASSOCIATED ANTIGENS IN HUMAN COLON CARCINOMAS XENOTRANSPLANTED INTO NUDE MICE (MEETING ABSTRACT)

Shochat D, Gold DV, Primus FJ, Dexter DL, Calabresi P, Goldenberg DM
Department of Pathology, University of Kentucky, Lexington, KY, 40536
Proc Am Assoc Cancer Res; 23:1086 1982

Human colon carcinoma produce several organ specific and tumor associated antigens, among them CEA (carcinoembryonic antigen), CSAp (colon-specific antigen P) and CMA. We have examined the antigen profiles of a number of different human colon carcinomas xenotransplanted into nude mice, to serve as a basis for use of these tumors as models for tumor antigen purification, radioimmunodetection, immunotherapy, etc. Extreme heterogeneity in antigen expression was observed by both radioimmunoassay and immunohistochemical procedures for each antigen. Four of 10 tumors (DLD-2, 3, 5 and HCT-10) were high producers of CEA. Two of these (DLD-2 and HCT-10) correlated with high production of CSAp and CMA, while the other two produced low quantities of CSAp and CMA. Another tumor (HCT14-OMI) produced large amounts of CMA, yet moderate amounts of CEA and low quantities of CSAp. Immunohistochemical analysis of CEA gave a mostly diffuse cellular and membranous staining for all of the tumors. Staining for CSAp was very focal, as for example in DLD-5 where only a few of the tumor cells were stained. In most cases staining for CMA was limited, however, DLD-2, HCT-10 and HCT 14 OMI showed intense intracellular and intraluminal staining. The data indicates that the various tumors differ, quantitatively and qualitatively in their expression of these antigens. (no Refs)

73. CARCINOEMBRYONIC ANTIGEN (CEA) RADIOACTIVE ANTIBODY FRAGMENTS FOR CANCER LOCALIZATION IN VIVO (MEETING ABSTRACT)

Gaffar SA, Bennett SJ, DeLand FH, Primus FJ, Goldenberg DM
University of Kentucky Medical Center, Lexington, KY, 40536
Proc Am Assoc Cancer Res; 23:985 1982

Previous experimental and clinical studies have indicated that radioactive antibodies to CEA can be used for the in vivo, external detection of CEA-producing tumors by the method of radioimmunodetection. These experiments involved the administration of affinity-purified, whole IgG goat antibody. In order to achieve a more rapid tumor accretion by a less immunogenic diagnostic reagent, the efficacy of F(ab')2 and Fab' fragments of the CEA antibody IgG were compared to that of whole antibody IgG and to normal goat IgG fragments. Tumor radiolocalization was evaluated in the GW-39 human colonic carcinoma growing in hamsters and producing CEA. In terms of antibody activity, the animals received concentrations of antibody fragments which were approximately equal to that of the intact antibody IgG, although a 50% reduction of CEA immunoreactivity was experienced in the preparation of Fab'. Tissue localization experiments (cpm/g) were performed at 1-14 hrs and 1-5 days after injection of the radioactive antibody preparations. Tumor localization (tumor/nontumor ratio) was higher for the native IgG antibody than for the antibody fragments or similar normal IgG preparations. The percentage of dose injected that was subsequently recovered in the tumor was 5-10 times higher for whole IgG antibody than for Fab', while the results for F(ab')2 were intermediate. These results suggest that whole IgG and F(ab')2 antibodies are the preferred preparations for tumor radioimmunodetection. (1 Ref)

74. TRANSPLANTATION IMMUNITY OF TWO CULTURED MURINE COLON LINES (MEETING ABSTRACT)

Sato N, Michaelides MC, Wallack MK
Department of Surgery, Washington University School of Medicine, St. Louis, MO, 63110
Proc Am Assoc Cancer Res; 23:1089 1982

In a search for the appropriate animal tumor model for human colon cancer, the chemically induced colon tumors 26 and 36 of BALB/c mice have been adapted to grow in vitro in our laboratory as C-C26 and C-C36, and their biologic activities have been characterized in vivo. The immunogenicity of these colon lines was investigated by injecting syngeneic mice with a tumorigenic dose of the cultured colon cells, excising the tumor which developed and subsequently challenging these animals, a week later, with serial doses of the same tumor, the other colon tumor, or with a syngeneic fibrosarcoma as a control. BALB/c mice immunized with these tumors resisted challenge with the same tumor as well as challenge with the other colon tumor, suggesting the presence of cross-reactive tumor rejection type antigens on these two cultured colon tumor lines. The immunobiologic characteristics of these two cultured colon tumors suggest that they may serve as useful models for studying colon cancer in the laboratory and for future immunoprotection and immunotherapy experiments. (no Refs)

75. INDUCTION OF COLORECTAL SQUAMOUS CELL CARCINOMAS IN RATS BY DEXTRAN SULFATE SODIUM.

Hirono I, Kuhara K, Yamaji T, Hosaka S, Golberg L
Dept. Carcinogenesis and Cancer Susceptibility, Inst. Medical Science, Univ. Tokyo, Shirokanedai 4-6-1, Minatoku, Tokyo 108, Japan
Carcinogenesis; 3(3):353-355 1982

ACI rats, 15 males and 15 females, were fed a diet containing 1% dextran sulfate sodium for 660 days. Twenty two of 29 surviving rats developed intestinal tumors between 288 and 660 days. Most tumors consisted of papillomas, and four squamous cell carcinomas were also induced, in addition to adenomas and adenocarcinomas. No intestinal tumors were observed in rats of the control group. (Author abstract) (5 Refs)

76. SURGICAL RESECTION OF THE RAT COLON: EFFECTS ON CARCINOGENESIS BY 1,2-DIMETHYLHYDRAZINE.

Rubio CA, Nylander G
Dept. Pathology, Karolinska Sjukhuset, Box 60500, Stockholm, Sweden S-104 01
JNCI; 68(5):813-815 1982

Following a 3-month treatment with 1,2-dimethylhydrazine (DMH) given weekly (sc), outbred Sprague-Dawley rats were subjected to partial resection of the transverse colon. After surgery, DMH treatment was continued for 6 months, after which the rats were killed. At autopsy, 63% of the tumors were found in the transverse colon. By contrast, only 29% of the tumors found in the 'sham-operated' control animals occurred in the transverse colon. Surgical trauma in the colon mucosa subjected to the action of carcinogenic agents appeared to promote the conditions suitable for the development of tumors in that organ. (Author abstract) (16 Refs)

77. BILE ACIDS: EFFECTS ON ABSORPTION OF 1,2-DIMETHYLHYDRAZINE AND 7,12-DIMETHYLBENZ[A]ANTHRACENE IN THE COLON OF THE RAT AND GUINEA PIG.

Rose RC, Nahrwold DL
Dept. Surgery, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
JNCI; 68(4):619-622 1982

The specific effects of bile acids as cocarcinogens were investigated. Absorptions of [14C]7,12-dimethylbenz[a]anthracene, [14C]dimethylhydrazine ([14C]DMH), and [3H]inulin from loops of colons from outbred Sprague-Dawley rats and Hartley guinea pigs were determined. In each animal absorption of one carcinogen and inulin was studied in one control loop and in a experimental loop containing either deoxycholic acid (DOC) or chenodeoxycholic acid (CDOC). DOC had a more pronounced effect on increasing loss of carcinogen from the intestinal lumen than did CDOC. This role of bile acids was consistent with their known effect of increasing intestinal permeability. Less carcinogen remained in the colon mucosa when DOC was present in the intestinal lumen. Although [14C]DMH was absorbed more rapidly from the intestinal lumina of guinea pigs than from those of rats, the rat accumulated more of the carcinogen in the intestinal mucosa and liver. (Author abstract) (16 Refs)

78. EFFECT OF ESTRADIOL PROPIONATE AND PREGNANCY ON CARCINOGENESIS INDUCED BY 1,2-DIMETHYLHYDRAZINE IN C3HA MICE.

Turusov VS, Murovannyi AN, Morozova OV
All-Union Cancer Res. Center, Moscow, USSR
Eksp Onkol; 4(2):20-23 1982

The effects of pregnancy and estradiol propionate (EP) administration on 1,2-dimethyl hydrazine (DMH)-induced carcinogenesis were studied in female C3HA mice. Virgin or pregnant females were subjected to sc administrations of DMH (8 mg/kg/wk) alone or in combination with EP (10 ug/kg/wk). DMH and EP were given for 30 wk. Animals were followed up for 50 wk after the initiation of the experiment. DMH alone induced tumors in 75% of virgin mice and in 56.2% of pregnant mice. EP administration resulted in a marked increase of the incidence of colonic tumors (31.6%, compared with 8.3% after administration of DMH alone to virgin mice and 18.7% after administration of DMH alone to pregnant mice). Uterine sarcomas were observed in 28.9% of mice treated with DMH + EP, while all mice treated with DMH alone were free of uterine sarcomas. Hepatocellular tumors were observed only in mice treated with DMH + EP (23.7%). These findings indicate that EP can modify the DMH-induced carcinogenesis not only in the hormone dependent organs but also in the liver and in the colon. (14 Refs) (In RUS)

79. THE KINETICS OF THE PROTECTIVE EFFECT OF BETA-SITOSTEROL AGAINST MNU-INDUCED COLONIC NEOPLASIA.

Deschner EE, Cohen BI, Raicht RF
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Cancer Res Clin Oncol; 103(1):49-54 1982

The effect of dietary supplementation with beta-sitosterol (0.2% of diet) was followed in Fischer rats after both acute and chronic feeding. Compared to controls after 3 and 7 days, the number of epithelial cells per crypt column in both plant sterol fed groups was shifted to lower values; moreover, fewer cells above cell position 12 were engaged in DNA synthesis. Continued feeding of beta-sitosterol for 28 wk revealed the number and position of 3HTdR-labeled cells per crypt column after 1 hr pulse labeling to be similar to that seen in the acute phase. However, differences were more marked after 24 hr showing the max number of labeled cells per column to be at least 25% less than the untreated group and the leading edge of labeled cells moving more slowly up the crypt wall. Rats treated with N-methyl-N-nitrosourea (MNU) intrarectally (8 mg/animal) while simultaneously consuming beta-sitosterol demonstrated a reduction in the size of the proliferative compartment as well as the number of labeled cells per crypt column as compared to rodents receiving just the carcinogen (3.3 and 5.4 mean labeled cells per column, respectively). At this time, MNU-treated rats fed beta-sitosterol had a significantly decreased colonic tumor incidence. This plant sterol which passes through the digestive tract relatively unabsorbed appears to slow colonic epithelial cell proliferation resulting in a reduced expression of neoplastic transformation. (Author abstract) (6 Refs)

80. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.

Larsen B
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Ugeskr Laeger; 144(12):860-863 1982

A review of studies on the biological effects of carrageenan shows that induction of colorectal cancer was observed in rats following long-term oral administration of degraded carrageenan. Native (high-molecular-weight) is not known to possess carcinogenic properties. Carrageenan stimulates tumor growth secondarily. The cocarcinogenic effect of carrageenan may be due to its immunosuppressive properties (toxic effect on macrophages and activation of macrophage suppressor cells). (29 Refs) (In DAN)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

81. FAMILY INCIDENCE OF CARCINOMA OF THE COLON AND RECTUM IN NORTH-EAST SCOTLAND.

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Gut; 23(2):169-171 1982

Family histories were obtained from 50 patients with adenocarcinoma of the colon or rectum in northeast Scotland. A comparable control group was similarly interviewed and in each group the case notes of the first degree relatives were studies where possible. Eight (16%) of the patients with cancer of the colon or rectum had a close relative with intestinal cancer compared with one (2%) of the control group. The patients with a positive family history of cancer of the large intestine did not have a higher proportion with adenomatous polyps nor were they younger than those patients with no such family history. (Author abstract) (12 Refs)

82. THE ASSOCIATION OF REMOTE STREPTOCOCCUS BOVIS BACTEREMIA WITH COLONIC NEOPLASIA.

Friedrich IA, Wormser GP, Gottfried EB
(c/o Wormser) Infectious Diseases Div., New York Medical College, Room 03, Westchester County Medical Center, Valhalla, NY, 10595
Am J Gastroenterol; 77(2):82-84 1982

We prospectively studied five patients with a remote history of Streptococcus bovis bacteremia who had not previously been evaluated for colonic pathology. This study was prompted by several reports of concomitant neoplasia in patients with recent S. bovis bacteremia. The patients were studied at a mean of 32 months after bacteremia. Despite the absence of other signs or symptoms suggestive of bowel disease, a negative test for occult blood in stool and a negative fecal culture for S. bovis, two patients were found to have neoplastic polyps of the colon. These findings suggest that the risk of colonic neoplasia in patients with remote S. bovis septicemia is similar to that found in patients with recent bacteremia, but evaluation of a larger group of these patients will be necessary to establish this risk. (Author abstract) (8 Refs)

83. RACIAL AND SOCIOECONOMIC STATUS DIFFERENCES IN SURVIVAL OF COLORECTAL CANCER PATIENTS IN HAWAII.

Wegner EL, Kolonel LN, Nomura AM, Lee J
Sociology Dept., Univ. Hawaii, Porteus 215, Honolulu, HI, 96822
Cancer; 49(10):2208-2216 1982

The study reported here examines the survival experience up to 84 mo of patients from the five major racial groups in Hawaii diagnosed with colorectal cancer during the yr between 1960 and 1974 based on data in the Hawaii Tumor Registry. Previous research in Hawaii showed that racial differences in survival existed even after adjusting for sex, age at diagnosis, stage of the disease at diagnosis, and normal life expectancy. In this paper, socioeconomic status differences between racial groups are hypothesized as a possible explanation for these survival differences. The results show that socioeconomic status did account for some survival differences between racial groups beyond what could be explained by the other variables. After adjusting for all the covariates, the only statistically significant racial differences which remained were higher survival rates for the Japanese patients compared with the rates for the Hawaiian and Filipino patients. Socioeconomic status was not found, however, to have a statistically significant effect on survival independent of race or the other variables examined. Reasons for the modest effects of socioeconomic status in this study are discussed. (Author abstract) (20 Refs)

84. MEAT AND FAT CONSUMPTION AND CANCER MORTALITY: A STUDY OF STRICT RELIGIOUS ORDERS IN BRITAIN.

Kinlen LJ
Cancer Res. Campaign, Cancer Epidemiology Res. Group, Univ. Oxford, Radcliffe Infirmary, Oxford, England
Lancet; 1(8278):946-949 1982

The close correlations between mortality from breast and colorectal cancers and the per-caput consumption of meat or fat in different countries suggest that these dietary items may be involved in the etiology of these neoplasms. To investigate further these possible relations a study has been conducted of cancer mortality between 1911 and 1978 in two groups of enclosed religious orders for women: one of 1,769 nuns who eat no meat and one of 1,044 nuns who eat little meat. Mortality from breast and colorectal cancer was not significantly lower in either group than in the general population. It is difficult to evaluate the small reduction in breast cancer mortality in the no-meat group because of the wide confidence limits. An unexpected finding was an excess mortality from esophageal cancer in both groups. These findings concern women who reduced their meat consumption in adult life: it is suggested that they are compatible with the evidence put forward to support a role for fat or meat intake in causation of breast cancer if dietary influences in pre-adult life are important. The findings on colorectal cancer point to the etiological importance in this disease of aspects of diet other than fat or meat intake. (Author abstract) (34 Refs)

85. FAECAL MUTAGENESIS AND COLONIC CANCER.

Askew AR, Ward M, Green MK, Reibelt LD
Dept. Surgery, Royal Brisbane Hosp., Herston 4029, Australia
Aust NZ J Surg; 52(1):27-29 1982

The incidence of fecal mutagens has been evaluated using the Ames Test in 16 patients with proven colon cancer and 35 volunteers with no symptoms referable to the colon and a negative hemoccult test. Twenty-five percent of the cancer patients, and 20% of the volunteers had mutagen positive feces. These results suggest that the incidence of fecal mutagens in patients with colon cancer is similar to that found in a population with a high risk of developing colonic neoplasms. (Author abstract) (8 Refs)

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OCTOBER, 1982

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. COLORECTAL CANCER: KNOWLEDGE AND ATTITUDES OF DOCTORS IN VICTORIA.

Macrae FA, Hill DJ, Dent O, Goulston KJ, StJohn DJ
(c/o St. John) Dept. Gastroenterology, Royal Melbourne Hosp., Royal Melbourne Hosp. Post Office, Melbourne, Victoria 3050, Australia

Aust NZ J Med; 12(3):278-283 1982

Successful introduction of screening for early colorectal cancer will depend, at least in part, on doctors' knowledge and attitudes. A 34-item questionnaire was sent to a random sample of one in five doctors in Victoria, with a final completion rate of 65%. The survey revealed gaps of knowledge, particularly about recognition of high-risk groups. Only 12% were aware of the degree of increased risk faced by first-degree relatives of patients with colorectal cancer and only 10% recognized the similar increase in risk for people with a history of resected colorectal cancer. While 73% of doctors order fecal occult blood tests, only 9% were aware that the more reliable guaiac method was used for their patients. Overall, 38% considered that fecal occult blood testing was a practical method for

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screening for colorectal cancer. Most of the doctors who accepted occult blood screening would follow up a positive test with digital rectal examination (80%) and barium enema (75%), but only 58% would want sigmoidoscopy performed and 34% colonoscopy. The diagnostic potential of digital rectal examination and sigmoidoscopy was over-estimated by half of the doctors surveyed. Recognition of subjects at high risk for colorectal cancer, and knowledge about the proper use, follow-up, and potential for screening of fecal occult blood tests need emphasis in medical educational programmes. (Author abstract) (30 Refs)

2. ENDOSCOPY IN OUTPATIENT PRACTICE.

Clemencon HG
Froheimweg 12, CH-4600 Olten, Switzerland
Internist (Berlin); 23(5):277-278 1982

Experience with diagnostic endoscopy in seven outpatient centers during the period 1974-1978 is reported. Gastric carcinoma was diagnosed in 902/25,337 patients subjected to upper panendoscopy. The overall incidence of gastric carcinoma was 7.0%, ranging from 5.8% to 9.2% during the 5 yr. Early gastric cancer accounted for 63/902 cases (12/130 in 1974, 10/172 in 1975, 13/181 in 1976, 12/178 in 1977 and 15/229 in 1978). The frequency of relevant diagnoses to (gastric and duodenal ulcers and gastric carcinoma) was 21.9% during the 5-yr period, ranging from 20.7% to 24.4%. Fiber colonoscopy was performed in 6,366 patients: colonic polyps were diagnosed in 1,224/6,366 patients (in 140/669 in 1974, 270/994 in 1975, 253/1,311 in 1976 and 300/1,702 in 1978). Colon carcinoma was diagnosed in 289/6,366 patients (4.54%: 5.8% in 1974, 6.7% in 1975, 3.9% in 1976, 3.6% in 1977 and 4.3% in 1977). The findings indicate that the incidence of endoscopic examinations and the percentages of gastroenterological diseases diagnosed are fairly constant in good outpatient practice. (16 Refs) (In GER)

3. COMPARATIVE STUDY OF ULTRASONOGRAPHY AND SCINTIGRAPHY IN LIVER METASTASES DETECTION IN CASES OF COLORECTAL CARCINOMA.

Arnaud JP, Daly R, Leguillou A, Adloff M
Service de Chirurgie, C.M.C.O., 19, rue Louis Pasteur, F 67300 Schiltigheim/Strasbourg, France
J Radiol; 63(2):97-100 1982

A comparative study has been realized to test the accuracy of ultrasonography and scintigraphy for detecting the presence of liver metastases in 305 patients with colorectal carcinomas. Presence or absence of hepatic metastases has been affirmed by laparotomy and biopsy. In the 47 cases with metastases, the sensitivity of ultrasonography was 93%, that of scintigraphy being 76%. In 258 cases without metastases the specificity of ultrasonography was 97%, that of scintigraphy being 92%. These results, confirmed by report in the published literature, show that ultrasonography should be the first examination for suspected hepatic metastases. (Author abstract) (24 Refs) (In FRE)

4. GASTROINTESTINAL TRACT CARCINOID: RADIOLOGIC AND PATHOLOGIC MORPHOLOGY.

Li S, Zou WZ, Xie JX, Zhu ST, Chen JC
Dept. Radiology, First Affiliated Hosp., Beijing Medical Coll., Beijing, People's Republic of China
Chin Med J [Engl]; 95(2):136-144 1982

Fifty-one cases (32 males and 19 females; 12-80 yr old, av age 41.4 yr) of gastrointestinal [GI] tract carcinoids are presented. Clinical, radiographic, and pathologic changes are reviewed. The distribution of lesion sites included stomach (15.7%), small bowel (29.4%), appendix (21.5%), colon (17.7%), and rectum (15.7%). Patients were categorized in 6 groups based on clinical criteria: abdominal with diarrhea, abdominal pain localized in right lower quadrant, intestinal obstruction symptoms with acute abdominal pain, massive upper GI tract bleeding, abnormal stool, and symptomless. Based on roentgenologic criteria the patients were categorized into 5 groups as follows: submucosal protruding lesions, filling defect in the GI tract with coexistence of extraluminal masses, pneumoperitoneum or intestinal intussusception, fungoid filling defect with infiltration of GI wall, and other signs. Metastatic carcinoids are composed of small cells,and atypia. Mitotic figures are infrequent. Metastases of carcinoid tumors were closely related to the size and site of the primary tumor. (8 Refs)

5. ANALYSIS OF THE CAUSES OF DELAYED DIAGNOSIS OF COLONIC CANCER.

Knysh VI, Prorokov VV, Ozhiganov EL, Barsukov IuA, Zaseev VK
All-Union Cancer Res. Center, Moscow, USSR
Klin Med (Mosk); 60(3):82-86 1982

To determine the causes of delayed diagnosis of colonic cancer, the case histories of 1,656 patients (600 men, 1,056 women; 20-79 yr old) with far advanced tumors were subjected to retrospective analysis. Among these patients, 51.5% had tumors of the left colon, 29.5% had tumors of the right colon, and 19.0% had tumors of the transverse colon. At primary examination, the disease was misdiagnosed in 38.9% of the patients. Initial diagnosis was of colitis (15.7%), gastritis or peptic ulcer (9.5%), cholecystopancreatitis or hepatitis (6.2%), acute appendicitis (1.5%), food poisoning (1.0%), or other diseases (5%). The causes of delayed diagnosis included the incomplete examination (25.8%), delay in seeking the medical help (18.4%), diagnostic errors (10.8%), and latent course of the disease (45.0%). It was emphasized that the patients with the history of villous polyps and adenomas should undergo annual examinations. Follow-up of the high risk patients should include colonoscopy, irrigoscopy with double contrasting, and the occult blood test. (16 Refs) (In RUS)

6. CAUSES OF LATE DIAGNOSIS OF RECTAL CANCER.

Knysh VI, Cherkes VL, Ozhiganov EL
All-Union Cancer Res. Inst., Moscow, USSR
Sov Med; (3):107-108 1982

To improve the early diagnosis of rectal cancer (RC), the case histories of 720 patients were subjected to a retrospective analysis. Among these patients, 28 were in Stage I, 107 were in Stage II, 355 were in Stage III, and 230 were in Stage IV. Duration of the symptoms ranged from 3-6 mo in 56% of the patients to greater than 6 mo in 44%. Delayed diagnosis of RC was associated with the latent course of the disease (6.8%), incomplete examination, refusal of the patient to undergo an extensive examination, and delayed seeking of the medical help. Diagnostic errors were observed in 271 patients. The disease was misdiagnosed for hemorrhoids, dysentery, colitis, anal fissure, and adnexitis. Diagnostic errors were the most frequent among the patients less than 40 yr old (47.5%, compared with 39.3% in 40-59 yr old age group, and 29.8% in the patients greater than 60 yr old). Of 272 patients with erroneous diagnosis, 212 had tumors of the rectal ampulla. (14 Refs) (In RUS)

7. PROSPECTIVE SURVEILLANCE BY RECTAL BIOPSY FOLLOWING ILEORECTAL ANASTOMOSIS FOR INFLAMMATORY DISEASE.

Khubchandani IT, Stasik JJ, Nedwich A
1275 South Cedar Crest Blvd., Allentown, PA, 18103
Dis Colon Rectum; 25(4):343-347 1982

A prospective study was designed to evaluate multiple rectal biopsy examinations for dysplasia in 34 patients who had ileorectal anastomosis performed, following colectomy for inflammatory bowel disease. Although all but 8 patients had persistent inflammatory activity on histologic examination, only one patient who demonstrated villous transformation of the mucosa clinically, showed carcinoma in situ in the excised rectal specimen. A protocol for surveillance of preserved rectums in inflammatory bowel disease is offered. (Author abstract) (18 Refs)

8. HUMAN LARGE-BOWEL CANCER: CORRELATION OF CLINICAL AND HISTOPATHOLOGICAL FEATURES WITH BANDED CHROMOSOMES.

Reichmann A, Levin B, Martin P
Dept. Medicine, Section Gastroenterology, Univ. Chicago, Box 400, 950 East 59th St., Chicago, IL, 60637
Int J Cancer; 29(6):625-630 1982

Clinical and histopathological features were correlated with cytogenetic banding studies on direct preparations from 31 large-bowel tumors. An interesting relationship between the site and the karyotypes of the tumors was observed. There appears to be a progressive increase in chromosomal number and/or structural rearrangement as one progresses from proximal to distal large bowel. We suggest that these observations may be related to differences in function and micro-environment within different areas of the colon. Although it is not known what factors favor cytogenetic variability and instability on the left side or the presence of fewer abnormalities on the right side of the colon, it is evident that clonal karyotypic evolution may be important in the progression of large-bowel cancer. The brevity of follow-up precludes conclusions regarding the influence of karyotype on survival. (Author abstract) (18 Refs)

9. CORRELATION BETWEEN IMMUNOLOGICAL TESTS AND PROGNOSIS IN PATIENTS WITH COLORECTAL AND PULMONARY TUMORS.

Stipa S, Schillaci A, Modini C
IV Cattedra di Patologia Chirurgica, Universita di Roma, Rome, Italy
Minerva Med; 73(18):1145-1148 1982

Correlations between some immunological parameters and prognosis were studied in patients with tumors. The carcinoembryonic antigen (CEA) levels were determined in 60 patients with colorectal cancer after surgery. The CEA levels were below 2.5 nanog (ng)/ml in 40/60 patients, and 2/40 of these patients subsequently developed recurrences. The incidence of recurrences was 9/20 among the 20/60 patients, with CEA levels exceeding 2.5 ng/ml. The spontaneous E, EA, Ea and EAC rosette formation was studied in 96 consecutive untreated patients with lung cancer compared with 75 healthy controls. Significant reduction of E, EA and EAC formation and less marked reduction of EA rosette formation were observed in the patients. Significant difference was found in the EAC rosette formation between the patients with adenocarcinomas and those with small-cell carcinomas. No significant difference was found in the immunological parameters between the patients in Stages I+II and III. (17 Refs) (In ITA)

10. IMMUNOHISTOCHEMICAL DETERMINATION OF THE CARCINOEMBRYONIC ANTIGEN IN CARCINOMA OF THE COLON.

de Beveraggi MT, Caccamo D
Servicio de Patologia, Hospital Italiano, Buenos Aires 1181, Argentina
Medicina (B Aires); 42(2):115-121 1982

Sixty patients bearing adenocarcinoma of the large bowel were evaluated immunohistochemically for the presence of the carcinoembryonic antigen (CEA) in the tumor and in the regional lymph nodes. The immunoperoxidase technique was utilized in the study of surgically resected specimens. A clear correlation was found between the amount of CEA present and the survival of the patient. Thus of the patients in the most advanced category (Dukes C), 66% of those with minimal CEA survived an av of 37 mo, 53% of those with medium amounts of CEA survived an av of 35 mo, and no patient with maximal amounts of CEA survived for more than an av of 9 mo. Survival to 18 mo for each category equaled 9/10, 11/14 and 1/10, respectively.Prognostic value of this technique was emphasized. (17 Refs) (In SPA)

11. DEMONSTRATION OF CARCINOEMBRYONIC ANTIGEN (CEA) BY MEANS OF THE IMMUNOPEROXIDASE TECHNIQUE IN PARAFFIN-EMBEDDED SPECIMENS OF TUMOUR TISSUES.

Heidl G
Institut fur Pathologie, Medizinische Akademie Carl Gustav Carus, Fetscherstrabe 74, DDR-8019 Dresden, W. Germany
Exp Pathol; 21(2):79-88 1982

The unlabeled antibody-enzyme method with the peroxidase-antiperoxidase complex (PAP-complex) was used to demonstrate carcinoembryonic antigen (CEA) or CEA-like substances in paraffin-embedded specimens of tumor tissues with an anti-CEA-antiserum of a rabbit. The anti-CEA-antiserum used in this study exhibited a high anti-CEA-activity and a low activity to an impurity. The paraffin-embedded specimens of tumor tissues were investigated at serum dilutions of 1:16, 1:64, and 1:256. The sections of colorectal cancer showed the highest content of CEA. In 36 of 37 cases the tumor tissue reacted to the anti-CEA-antiserum up to a dilution of 1:256. The stomach cancer tissues contained significantly lower CEA-levels than the colorectal cancer. The sarcomas, malignant melanomas, the tumor of testis, the prostatic cancers and basal cell carcinoma of the skin were found to contain none or very low CEA-content. In most specimens of these tumors the CEA was not demonstrable at a 1:16 dilution of the primary antiserum. (Author abstract) (49 Refs)

12. ESTROGEN RECEPTOR PROTEIN IN ADENOMAS OF THE LARGE BOWEL.

Agrez MV, Spencer RJ
(c/o Spencer) Dept. Colorectal Surgery, Mayo Clinic, 200 First St. Southwest, Rochester, MN, 55905
Dis Colon Rectum; 25(4):348-350 1982

Thirty adenomas of the large bowel, removed from 15 females and 15 males, were examined for the presence of estrogen receptor protein. The finding of positive binding capacity in 2 of the 30 adenomas supports the hypothesis that hormonal dependency does not play a major role in the development and growth of colorectal adenomas. (Author abstract) (15 Refs)

13. HORMONE RECEPTORS IN COLON CANCER.

Zannini G, Contieri E
II Facolta di Medicina e Chirurgia, Universita di Napoli, Naples, Italy
Minerva Med; 73(18):1221-1224 1982

The hypothesis on the presence of specific hormone receptors in neoplasms of the colon was tested in 12 patients with primary multiple malignant tumors and on the effectiveness of adjuvant hormone therapy of 20 patients with inoperable malignant tumors of the digestive tract. Three of the 12 patients with primary multiple tumors had synchronous tumors, and the 9 others had metachronous tumors. Two of the three patients with synchronous tumors had adenocarcinomas of the colon and rectum, respectively, the third had carcinomas. In the nine patients with diachronous tumors the first tumors were located in the breast, larynx, uterus, ovary, thyroid gland and stomach, and the second tumors in the breast, colon, rectum, and sigmoid colon. The group of 20 patients (10 men and 10 women) with inoperable tumors were randomized into two groups. One group was (Group I) subjected to cyclic polychemotherapy, the other (Group II) to cyclic polychemotherapy with medroxyprogesterone acetate (MPA: 1,000 mg/day po). The evaluation after 12 mo showed an improvement concerning anorexia in 20% of the patients in Group I and in 70% in II, concerning dysphagia in 20% and 40%, concerning emesis in 10% and 40%, concerning asthenia in 20% and 70%, concerning pain in 20% and 60%, and concerning ability to work in 20% and 60%, respectively. The 1-yr survival rate were 30% in Group I and 70% in Group II. The findings indicate the effectiveness of adjuvant MPA therapy. (10 Refs) (In ITA)

14. ANTIBODIES TO INTERMEDIATE FILAMENTS AS DIAGNOSTIC TOOLS: HUMAN GASTROINTESTINAL CARCINOMAS EXPRESS PREKERATIN.

Altmannsberger M, Weber K, Holzcher A, Schauer A, Osborn M
(c/o Osborn), Max-Planck-Institute for Biophysical Chemistry, D-3400 Goettingen, W. Germany
Lab Invest; 46(5):520-526 1982

Twenty-five primary gastrointestinal carcinomas have been studied using immunofluorescence microscopy with affinity-purified antibodies to prekeratin and to vimentin. The tissues were alcohol fixed and paraffin embedded before use. In all cases (ie, 1 case of esophageal carcinoma, 7 stomach carcinomas, and 17 large bowel carcinomas) the tumor cells are stained by antibodies to prekeratin. In cases in which only very few tumor cells are present, such as signet ring carcinoma, immunofluorescence with prekeratin antibody provides an easy way to visualize single tumor cells. When the same specimens were tested with antibodies to vimentin, the tumor cells were unstained, and only the fibroblasts and vessels of the stroma were decorated. Four of the tumors were also negative when tested with antibodies specific for either desmin, or glial fibrillary acidic protein or neurofilaments. Three metastases to the abdominal region from tumors originating in the ovary, stomach, and large bowel were like the primary tumors in that the tumor cells were positive when stained with antibodies to prekeratin and negative when tested with the antibodies to vimentin. (Author abstract) (25 Refs)

15. ENZYMATIC CHARACTERISTICS OF TUBULAR ADENOMAS AND CARCINOMAS OF THE LARGE INTESTINE.

Vatn MH, Tjora S, Arva PH, Serck-Hanssen A, Stromme JH
Med A, Rikshospitalet, Oslo 1, Norway
Gut; 23(3):194-197 1982

Enzyme activities in homogenates of the large intestine were measured in biopsies from 11 tubular adenomas and 6 carcinomas and from the corresponding normal mucosa of each individual. A similar and significant increase was found in the total activities of glucose-6-phosphate dehydrogenase (G-6-PD), pyruvate kinase, and lactate dehydrogenase in adenomas and carcinomas as compared with levels of normal mucosa. The lactate dehydrogenase isoenzyme patterns showed also a marked and similar change in the adenomas and carcinomas with a significant increase of lactate dehydrogenase M-monomers. Most of the adenomas showed slight to moderate dysplasia. The results indicate that the measurement of total G-6-PD, pyruvate kinase and lactate dehydrogenase activities for screening purposes has no predictive value in separating nonpremalignant from premalignant adenomas. Moreover, it seems that the enzymatic characteristics of malignancy are present even in tubular adenomas. This is in agreement with the theory of a polyp-cancer sequence. (Author abstract) (25 Refs)

16. PRESENTATION OF MALIGNANT LYMPHOMA IN THE RECTUM.

Heule BV, Taylor CR, Terry R, Lukes RJ
(c/o Lukes) Dept. Pathology, Section Hematopathology, Univ. Southern California Sch. Medicine, 2025 Zonal Ave., Los Angeles, CA, 90033
Cancer; 49(12):2602-2607 1982

Because of their rarity, rectal malignant lymphomas are generally included in the group of large intestine lymphomas. A study of eight cases of rectal lymphomas revealed distinctive clinicopathologic correlations. Using the Lukes-Collins classification of malignant lymphomas, the authors interpreted all the cases as B-cell lymphomas, supported by immunologic studies in four cases. Seven cases were classified diffuse follicular center cell (FCC) lymphomas; four as small cleaved FCC; and three as small noncleaved FCC. One case was interpreted as plasmacytoid lymphocytic lymphoma. Monoclonality was demonstrated by immunoperoxidase staining of cytoplasmic immunoglobulin in three cases and by immunologic surface marker studies in another case. The small noncleaved follicular center cell lymphomas presented as localized tumors (clinical Stage I), so-called primary lymphomas. The small cleaved follicular center cell lymphomas, by contrast, were part of a generalized lymphomatous process in three of the four cases with demonstrated involvement of the gastrointestinal tract elsewhere in two cases. (Author abstract) (17 Refs)

17. KRYPTO-HAEM-SSW, A TEST TAPE FOR DETECTION OF OCCULT BLOOD IN STOOL.

Lampe J, Jacobasch KH, Uhlig K
Abteilung Hamkatalyse, Zentralinstitut fur Molekularbiologie der Akademie der Wissenschaften DDR, Lindenberger Weg 70, DDR-1115 Berlin-Buch, E. Germany
Dtsch Gesundheitswes; 37(4):175-177 1982

The author reports the results of analytical and clinical investigations with Krypto-Haem SSW, a test tape for the detection of occult blood in the feces. In laboratory tests this test tape detected hemoglobin concentrations of 2 mg/g feces. The rate of false-negative tests, in 72 patients with colon-rectum carcinoma amounted to 26.4%. Out of 82 patients with polyps 75.6% showed a false-negative result. However, most of these were smaller polyps. In healthy subjects false-positive reactions were found in less than 1.6%. Comparative studies with the hemocculttest indicate a somewhat higher sensitivity of Krypto-Haem SSW. Krypto-Haem SSW is recommended as screening-test for the early detection of carcinoma of colon and rectum. (Author abstract) (17 Refs) (In GER)

18. FAECAL OCCULT BLOOD TESTING FOR COLORECTAL CANCER IN GENERAL PRACTICE.

Million R, Howarth J, Turnberg E, Turnberg LA
Dept. Medicine, Univ. Manchester Sch. Medicine, Hope Hosp., Eccles Old Road, Salford M6 8HD, England
Practitioner; 226(1366):659-660,663 1982

The acceptability of fecal occult blood testing (FOBT) was examined in three general practices in an industrial city (Salford, England). Of 5,812 people contacted, only 28.3% agreed to take part and of this number, 2.3% had one or more positive FOBT. Two colonic cancers were diagnosed, as were five patients with adenomatous polyps. The influence of age, social class and improved education programs on FOBT are discussed, along with possible cost estimates of such a program. (16 Refs)

19. BIOLOGICAL MARKERS AS AN AID IN THE CLINICAL MANAGEMENT OF PATIENTS WITH LIVER METASTASES.

Waalkes TP, Abeloff MD, Ettinger DS, Mrochek JE, Bostick WD
Johns Hopkins Oncology Center, Room 167, 600 North Wolfe St., Baltimore, MD, 21205
J Surg Oncol; 20(2):83-94 1982

Liver metastases due to the more common neoplastic diseases such as colorectal, breast, or bronchogenic carcinoma are a frequent occurrence and are associated with an ominous prognosis. Earlier detection followed by appropriate therapeutic interventions might have a decided effect on the subsequent course of disease. Controversy exists over the selection of tests with the greatest sensitivity, specificity, and potential utility. Preliminary evidence suggest that gamma-glutamyl transpeptidase and 5'-nucleotidase may be of particular significance. Four enzymes - gamma-glutamyl transpeptidase, 5'-nucleotidase, leucine aminopeptidase, and alkaline phosphatase plus carcinoembryonic antigen - were compared in the same blood samples from selected patients with breast and small cell carcinoma of the lung. Gamma-glutamyl transpeptidase was the most sensitive test with 28/29 (97%) patients with hepatic metastases having elevated enzymatic activity in their sera. For patients with small cell carcinoma of the lung followed serially, gamma-glutamyl transpeptidase activity was increased an average of 5 months before liver metastases were detected by clinical means. Two factors are important in the interpretation of the results of gamma-glutamyl transpeptidase analysis: (1) Hepatic dysfunction due to diseases other than metastatic tumor involvement can cause a rise in enzyme levels as can (2) medications or ethanol which activate the hepatic microsomal drug metabolizing system. Of particular importance, however, is the fact that antitumor chemotherapy, even intensive and multiple agent, did not appear to effect the enzyme activity in the sera of patients with breast or small cell carcinoma of the lung. Gamma-Glutamyl transpeptidase in combination with carcinoembryonic antigen may be of particular value in detecting liver metastases and in assessing subsequent response to therapy. (Author abstract) (45 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

20. RADICAL RESTORATIVE SURGERY FOR POORLY DIFFERENTIATED CARCINOMA OF THE MID-RECTUM.

Elliot MS, Todd IP, Nicholls RJ
(c/o Nicholls), St. Mark's Hosp., City Road, London EC1V 2PS, England
Br J Surg; 69(5):273-274 1982

A retrospective study was made to compare the results of restorative surgery with those of total rectal excision in the treatment of patients with a poorly differentiated adenocarcinoma of the middle third of the rectum (between 8 and 12 cm from the anal verge). Of 1,163 patients presenting between 1963 and 1975, 42 with poorly differentiated tumors at this level were followed up after treatment by a radical (ie curative) operation. Twenty-eight underwent total rectal excision and 14 anterior resection. Examination of the preoperative biopsy correctly established the histological grade in 17 (40%) of 42 cases. Pathological examination of the resected specimens showed a slightly higher proportion of Dukes' C2 tumors and those with venous invasion removed by total rectal excision, but the extent of local spread among tumors removed by either operation was similar. There was no operative mortality. Ten out of 28 patients treated by total rectal excision (36%) and 6 out of 14 treated by anterior resection (43%) were alive at 5 yr. One patient developed a histologically proved local recurrence after anterior resection; no other proved local recurrence was recorded. It would appear, therefore, that where radical surgery is possible, anterior resection offers as good a prospect of cure as total rectal excision for poorly differentiated tumors of the mid-rectum. (Author abstract) (8 Refs)

21. LONG TERM RESULTS OF RESTORATIVE RESECTION AND TOTAL EXCISION FOR CARCINOMA OF THE MIDDLE THIRD OF THE RECTUM.

McDermott F, Hughes E, Pihl E, Milne BJ, Price A
Dept. Surgery, Monash Univ., Alfred Hosp., Prahran, Victoria, Australia
Surg Gynecol Obstet; 154(6):833-837 1982

Restorative resection for carcinoma of the middle third of the rectum has been facilitated by the recent introduction of the staplers. Before restorative resection with end-to-end anastomosis can become the treatment of choice, it must be proved that survival prospects after restorative resection are similar to those obtained after total abdominoperineal excision. The results of curative restorative resection and total excision in 417 patients with a single carcinoma of the middle third of the rectum managed by one of us are examined. Between 1950 and 1980, the proportion of patients treated by restorative resection for carcinoma of the middle third of the rectum increased from 26 to 93%. Distribution by sex, age, tumor stage and tumor differentiation did not differ significantly between the two groups of patients operated upon. Cancer specific survival did not differ significantly between patients treated by restorative resection or total excision. Ten yr survival rates were 60 and 59%, respectively. Survival related to tumor stage and differentiation was not influenced by the type of operation. Tumor size, greater - p less than 0.04-in patients managed by total excision, had no significant influence on survival prospects. The results justify sphincter preservation and suggest that increased usage of restorative resection by stapling techniques is not likely to lessen survival prospects in patients with carcinoma of the middle third of the rectum. (Author abstract) (9 Refs)

22. POSTERIOR SURGICAL APPROACHES TO THE RECTUM.

Westbrook KC, Lang NP, Broadwater JR, Thompson BW
Dept. Surgery, Univ. Arkansas Medical Sciences, 4301 West Markham St., Little Rock, AR, 72205
Ann Surg; 195(6):677-685 1982

This report summarizes experience with 19 posterior approaches to the rectum including 9 trans-sacral (Kraske) and 10 trans-sphincteric (Mason) procedures. This study included 12 men and 7 women, ranging in age from 18 to 89 yr. Surgical indications included villous tumors in nine patients, various benign problems in four patients, primary carcinomas in three patients, and recurrent cancer in three patients. Eight complications developed in the 19 patients including: four fecal fistulae, two wound dehiscences, one rectal stricture, and one sacrococcygeal hernia. Spontaneous closure of the fecal fistulae occurred in two patients, and two patients required proximal colostomies. Fecal continence was achieved in 18 of the 19 patients. No patient died as a complication of the procedure. No recurrent tumors have developed. The conclusion is that a posterior approach to the rectum is a safe and effective procedure for various benign and for selected malignant conditions. It is particularly suitable for villous tumors that are too high for transanal resection and too low for transabdominal resection. It is an effective procedure for small, exophytic, mobile carcinomas of the lower 10 cm of the rectum in selected patients. (Author abstract) (18 Refs)

23. THE EFFECTIVENESS OF WIDE ANATOMICAL RESECTION AND RADICAL LYMPHADENECTOMY FOR PATIENTS WITH RECTAL CANCER.

Hojo K, Koyama Y
Dept. Surgery, Natl. Cancer Center Hosp., 5-1-1 Tsukiji, Chuoh-ku, Tokyo 104, Japan
Jpn J Surg; 12(2):111-116 1982

Wide anatomical resection with extensive en bloc dissection of lymph nodes was used to treat 113 Japanese patients (Group 1) with rectal cancer during the period 1969-1976, and the results were compared with those obtained by conventional surgery (upper dissection is made around the origin of the upper rectal artery without any systematic lateral dissection or extended dissection in the perineal side) in 119 patients during the same time period (Group 2) and in 160 patients treated during the period 1962-1968 (Group 3). The cumulative 5-yr survival rates for Groups 1, 2, and 3 were: 90.3, 67.8, and 70%, respectively, for patients classified as Dukes B and 51.6, 37.8, and 26.3%, respectively, for patients classified as Dukes C. The incidences of local recurrence for Groups 1 and 2 were 6.5 and 25%, respectively, for Dukes B patients and 45.5 and 25%, respectively, for Dukes C patients. In Dukes C patients, the incidences of postoperative distant metastases for Groups 1 and 2 were 27 and 22.7%, respectively, indicating no significant difference. However, the differences in 5-yr survival rates and incidence of local recurrence between conventionally treated and extensively treated patients were significant. (5 Refs)

24. EEA STAPLER IN LOW ANTERIOR ANASTOMOSIS.

Vezeridis M, Evans JT, Mittelman A, Ledesma EJ
(c/o Ledesma), Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Dis Colon Rectum; 25(4):364-367 1982

Preservation of the anal sphincter is a goal of all surgeons treating colorectal malignancies. In the hands of many, transsacral and low anterior resections with end-to-end anastomosis have been associated with high morbidity and leakage. The EEA stapler represents an alternative in reestablishing bowel continuity. Fifty-eight patients with adenocarcinoma of the rectum were treated over a 3-yr period at Roswell Park Memorial Institute. Forty-nine procedures judged to be curative and 9, palliative. All patients had an EEA stapler introduced through the anus. No protective colostomies were needed. No case of clinically significant anastomotic leakage was seen. Minor spotting or bleeding was documented, but no patient required blood transfusions. Two patients developed constipation; 16 patients had temporary soiling, 2 had prolonged soiling. Frank incontinence was not observed. The EEA stapler is an evolutionary instrument derived from the Russian PKS model. It is safe, reliable, and simple to operate. With adequate training of the surgeon, precious time can be saved. Intraoperative sigmoidoscopies, as well as postoperative barium enema examinations, were not needed. Gaps in the stapled anastomotic line (when present) were easily repaired. It is too early to tell whether anastomotic and local recurrence rates will increase, as more sphincter-saving procedures were performed. Five-yr follow up is crucial to establish criteria for the use of EEA stapler. (Author abstract) (13 Refs)

25. SEPSIS AND ASEPSIS IN LARGE BOWEL CANCER SURGERY.

Hughes ES, McDermott FT, Polglase AL, Johnson WR, Phil EA
Dept. Surgery, Monash Hosp., Alfred Univ., Commercial Road, Prahran, 3181 Victoria, Australia
World J Surg; 6(2):160-165 1982

Current practices for preventing infection after surgery for large bowel cancer are reviewed. Sepsis causes just over one-fourth of the deaths in this type of operation. Current practice involves any combination of reducing microorganisms in the bowel, reducing contamination of the wound, and destroying microorganisms in the wound. Strict attention should be paid to aseptic technique. Preoperative cefazolin (1 g) and metronidazole (1.2 g) may be useful. (17 Refs)

26. INTESTINAL ANTISEPSIS: RATIONALE AND RESULTS.

Condon RE
Dept. Surgery, Medical Coll. Wisconsin, Milwaukee, WI, 53226
World J Surg; 6(2):182-187 1982

Good results were achieved in preventing septic complications from colorectal surgery with an intensive oral preoperative regimen of neomycin and erythromycin. Septic complications occurred in 28/60 patients given placebo, as compared to 5/56 given the antibiotic regimen (p less than 0.05). A review of other studies indicates that an oral aminoglycoside in combination with an anaerobic agent gives good results. The combination used here is recommended because it is less expensive, less toxic, and the emergence of resistant organisms has not been observed. (25 Refs)

27. THE INFLUENCE OF ANTIBIOTICS ON INFECTION AND ANASTOMOTIC RECURRENCE AFTER COLON RESECTION FOR CANCER.

Herter FP
161 Fort Washington Ave., New York, NY, 10032
World J Surg; 6(2):188-194 1982

The effect of antibiotic treatment on occurrence of infection after colorectal resection and anastomosis for cancer was reviewed in 230 cases treated from 1975-1977 by 25 surgeons. Infection occurred in 16.5% overall: in 32% of 67 patients receiving no antibiotics; in 9.8% of 163 patients receiving some form of antibiotic prophylaxis; in 6.9% of 72 patients receiving systemic perioperative antibiotic therapy; and in 3.1% of 32 patients receiving preoperative oral and perioperative antibiotic therapy. Antibiotic therapy was not associated with postoperative enterocolitis. (12 Refs)

28. INDICATION AND POTENTIALS OF SURGICAL THERAPY OF HEPATIC METASTASES.

Horn J
Chirurgische Klinik, Universitat Heidelberg, Im Neuenheimer Feld 110, D-6900 Heidelberg, W. Germany
MMW; 124(13):312-316 1982

Surgical resection of hepatic metastases (HM) can in some cases increase survival time. HM develop most frequently from malignancies of the gastrointestinal tract. Prognosis is most favorable when the primary tumor can be curably resected. Five-yr survival is 30% for solitary HM and 13% for multiple HM. Prognosis becomes more favorable as the length of the interval between resection of the primary tumor and development of HM increases; the presence of metastases at the time of diagnosis of the primary tumor is an indication of advanced disease. HM of colorectal cancers carry a better prognosis than do HM of other tumors. Cure requires complete removal of HM; however, extended radical surgery does not increase survival when compared with more conservative surgery. Ligature of the hepatic artery, in spite of apparent theoretical advantages, has not resulted in effective control of growth of HM. Some studies, difficult to confirm, indicate that local cytostatic therapy can lengthen survival time and reduce the severity of symptoms. Current data are insufficient to determine the value of combining hepatic perfusion of cytostatic agents with ligation of the hepatic artery. (52 Refs) (In GER)

29. THE USE OF IRRADIATION THERAPY IN THE TREATMENT OF TUMORS OF THE RECTUM AND RECTOSIGMOID.

Saxton JP, Withers HR, Romsdahl MM, Borgelt BB
Dept. Radiotherapy, M. D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030
J Natl Med Assoc; 74(6):529-533 1982

As a means of increasing local control and disease-free survival in patients with carcinoma of the rectum and rectosigmoid, preoperative and postoperative irradiation therapy have been shown to be effective. The question of the sequence of delivering adjuvant radiation therapy is not settled; however, the benefits and deficits of irradiation therapy as an adjuvant to surgery preoperative and postoperative are reviewed. Basic principles of radiation oncology affecting the selection of the sequence and technique of treatment are discussed. (Author abstract) (25 Refs)

30. PREOPERATIVE RADIATION AND CHEMOTHERAPY FOR ANAL AND RECTAL CANCER..

Smith DE, Muff NS, Shetabi H
1023 South Third St., Mount Vernon, WA, 98273
Am J Surg; 143(5):595-598 1982

It became apparent on review of the recent literature that the combination of radiation therapy and chemotherapy may offer increased response in patients with locally advanced carcinomas of the anus and rectum. The protocol for this group is 1 wk of chemotherapy with 3 wk of radiation, followed 3 to 6 wk later by surgical intervention. In this limited group of 10 patients, considerable benefit was noted. All of the lesions decreased dramatically in size, with 8 of the 10 patients showing more than a 50% decrease. Only 1 of the 10 patients showed evidence of nodal involvement at the time of surgery. Three of the patients showed no evidence of tumor and three others showed microscopic tumor only. While the number of patients is small and follow-up is still short, the study seems to have shown the same improved results which have been reported by others using similar protocols. If our long-term follow-up remains equally satisfactory, then the concept of low dose drug therapy combined with radiation could have broader implications, and perhaps be extended to other neoplastic diseases with the same excellent tolerance. This form of therapy can be provided in the setting of a community cancer center, where radiation therapy and medical oncology services are available as an adjunct to surgery. (Author abstract) (12 Refs)

31. THE COMBINATION OF 5-FLUOROURACIL WITH MISONIDAZOLE IN PATIENTS WITH ADVANCED COLORECTAL CANCER.

Spooner D, Bugden RD, Peckham MJ, Wist EA
Div. Radiotherapy, Royal Marsden Hosp., Belmont, Surrey, SM2 5PT, England
Int J Radiat Oncol Biol Phys; 8(3/4):387-389 1982

The demonstration that misonidazole (MISO, 1 g/kg) produced a 1.6 fold increase in cell killing of im Lewis lung carcinoma in mice when administered simultaneously with 5-fluorouracil (FU) prompted a Phase I study of the MISO/FU combination in 15 advanced colorectal cancer patients. Patients were allocated to received a combination of FU [1.0 g/square meter (m2), iv bolus 4 hr post-MISO] with either MISO 2 g/m2 po (7 patients) or 3 g/m2 po (8 patients). Courses were given at 21-day intervals to a maximum cumulative MISO dose of 12 g/m2. Gastrointestinal side effects were more frequent and more severe in patients receiving MISO/FU versus FU alone. Leukopenia incidence was similar for both treatment regimens and no CNS or peripheral neuropathy was observed for either protocol. Simultaneous administration of FU did not modify 24 hr plasma nitroimidazole pharmacokinetics. Objective tumor responses, one complete and one partial, were observed in 2/9 (22%) patients receiving two or more courses of MISO/FU. MISO and FU can apparently be combined without serious pharmacokinetic or toxicologic complications. The potential value of MISO/FU in terms of tumor response in large bowel adenocarcinoma will be examined in the future. (14 Refs)

32. PHASE I-PHASE II TRIAL OF N-PHOSPHONACETYL-L-ASPARTIC ACID GIVEN BY INTRAVENOUS INFUSION AND 5-FLUOROURACIL GIVEN BY BOLUS INJECTION.

Erlichman C, Donehower RC, Speyer JL, Klecker R, Chabner BA
Dept. Medicine, Princess Margaret Hosp., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada
JNCI; 68(2):227-231 1982

A phase I clinical trial of N-phosphonacetyl-L-aspartic acid (PALA) and 5-fluorouracil (FUra) was performed on 30 patients. PALA was given as a 15-min iv infusion once daily for 5 days, and FUra was given as a bolus injection on days 2, 3, 4, and 5. Cycles of treatment were repeated every 3 wk. Dose-limiting toxicity was manifested by stomatitis and diarrhea. Skin rash was observed also but was not dose limiting. No consistent hematopoietic or renal toxicity was observed. Seventeen patients with disseminated metastatic melanoma and measurable disease were evaluated for response. One partial response was seen; however, the response was associated with significant toxicity, and the treatment could not be repeated. Stable disease was observed in 3 patients with melanoma, 1 patient with colon carcinoma, and 1 patient with ovarian carcinoma. Our findings suggest that the clinical activity of PALA and FUra given according to the above schedule for melanoma is less than 25% (p less than 0.05). Pharmacokinetic studies of FUra revealed no consistent effect of PALA pretreatment on FUra disappearance in plasma. the mean FUra elimination half-life in plasma was 7.11 +-0.84 min (SEM), which is no different from that reported for FUra alone. The recommended doses on this schedule for phase II studies are 1,000 mg PALA/m(2)/day iv daily for 5 days and 200 mg FUra/m(2)/day iv on days 2, 3, 4, and 5. (Author abstract) (19 Refs)

33. 5-FU AND ALLOPURINOL: TOXICITY MODULATION AND PHASE II RESULTS IN COLON CANCER.

Kroener JF, Saleh F, Howell SB
Scripps Clinic and Res. Foundation, 10666 N. Torrey Pines Road, La Jolla, CA, 92037
Cancer Treat Rep; 66(5):1133-1137 1982

Concurrent administration of allopurinol allows escalation of 5-fluorouracil doses in man when 5-FU is given by continuous infusion for 5 days. Forty-nine patients received 81 courses of treatment with 5-FU and allopurinol in Phase I and II trials. The dose-limiting toxicity was mucositis; marrow toxicity was mild. Neurotoxicity, possibly related to 5-FU, occurred in eight patients. No responses were seen in 14 evaluable patients with colon cancer, 11 of whom had had prior 5-FU. One patients with Hodgkin's disease had a partial response; one patient with diffuse histiocytic lymphoma had transient disease regression. Although allopurinol does modify the toxicity of 5-FU, permitting dose escalation, it does not increase the therapeutic index in colon cancer. Infusional 5-FU deserves further study in lymphoma. (Author abstract) (22 Refs)

34. CLINICAL PHARMACOLOGICAL STUDIES OF CONCURRENT INFUSION OF 5-FLUOROURACIL AND THYMIDINE IN TREATMENT OF COLORECTAL CARCINOMAS.

Au JL, Rustum YM, Ledesma EJ, Mittelman A, Creaven PJ
Dept. Experimental Therapeutics, Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(7):2930-2937 1982

The effects of thymidine (dThd) coadministration on the pharmacokinetics and metabolism of 5-fluorouracil (FUra) were investigated in 29 colorectal cancer patients. Five patients received 5-day iv infusion of FUra and 24 patients received infusion of FUra and dThd preceded by a bolus dose of dThd. Plasma and urine concentrations of FUra, 5-fluorodeoxyuridine (FdUrd), thymine, and dThd were quantitated by a high pressure liquid chromatography. Concurrent dThd administration reduced the plasma clearance of FUra at steady state. Plasma concentrations of FUra were linearly dependent on those of thymine. Results indicated that the elimination of FUra was reduced by thymine. In contrast to the absence of FdUrd as a circulating metabolite in patients treated with FUra alone, uM concentrations of FdUrd were detected in plasma of most of the patients treated with FUra-dThd. This together with the liner correlation of FdUrd and dTHd concentrations indicates that the interconversion of the FUra to FdUrd was enhanced by dThd. The incidence of dose-limiting leukopenia in the FUra-dThd combination therapy was 40%. There is an inverse correlation between the plasma clearance concentration of FUra at steady state and hematological toxicity. The biochemical effects of dThd on the incorporation of FUra and FdUrd into RNA and into acid-soluble 5-fluorodeoxyuridine monophosphate (FdUMP) in human colon tumor cells were studied in vitro. The response rate of colorectal carcinoma to FUra was not improved by coadministration of dThd; only one of the 11 patients who had no prior FUra therapy achieved partial remission. The lack of clinical response in these patients may be partly due to the inhibition of anabolism of FUra and FdUrd to FdUMP by dThd. (26 Refs)

35. ADENOCARINOMA OF THE COLON WITH HEPATIC METASTASES. FIFTEEN-YEAR SURVIVAL.

Levine AW, Donegan WL, Irwin M
(c/o Donegan) Dept. Surgery, Medical Coll. Wisconsin, 8700 West Wisconsin Ave., Milwaukee, WI, 53226
JAMA; 247(20):2809-2810 1982

Twenty patients with colon adenocarcinoma metastatic to the liver were treated with fluorouracil iv or po. Six patients received other agents, including carbomycin, mitomycin, busulfan, stanozolol, and toyocamycin. Median survival time was 11.5 mo. Eight patients lived greater than 1 yr, and three lived greater than 2 yr. Excluding the patient who survived almost 15 yr, the av longevity was 12.4 mo. One patient, a 44-yr-old woman, underwent 13 yr of fluorouracil treatment (5 iv injections/mo) for secondary liver adenocarcinoma following limited resection of an adenocarcinoma of the ascending colon. Eventually the patient developed episodic jaundice followed by common bile duct obstruction, hepatic abscesses, and recurrent biliary tract obstruction. The patient died almost 15 yr after the detection of liver metastases. Use of fluorouracil for the treatment of secondary liver adenocarcinomas is discussed. (10 Refs)

36. AN APPRAISAL OF TRANSCATHETER ARTERIAL EMBOLIZATION COMBINED WITH TRANSCATHETER ARTERIAL INFUSION OF CHEMOTHERAPEUTIC AGENT FOR HEPATIC MALIGNANCIES.

Okamura J, Horikawa S, Fujiyama T, Monden M, Kambayashi J, Sikujara O, Sakurai M, Kuroda C, Nakamura H, Kosaki G
Second Dept. Surgery, Fukushima, Fukushima-ku, Osaka 553, Japan
World J Surg; 6(3):352-357 1982

Use of transcatheter arterial embolization (TAE) combined with transcatheter arterial infusion (TAI) of chemotherapeutic agents in 68 patients (63 men, 5 women; 30-79 yr old) with hepatic malignancies is reported. In cases with a hypervascular tumor and a patent portal vein, 40-60 mg of adriamycin or 10 mg of mitomycin were infused through the same catheter. Ten to 15 min later, Gelfoam particles immersed with adriamycin (10 mg) were injected into the intrahepatic branch of the hepatic artery. Occlusion was confirmed by angiography. Two to 3 wk later, the tumor mass was reexamined and hepatic lobectomy or local excision or segmental resection were performed. Of the 68 tumors, 58 were considered unresectable. Six mo and 1-yr actuarial survival rates of these 58 patients were 69.7% and 56.2%, respectively. Ten patients (8 men, 2 women; 52-69 yr old) underwent elective hepatic resection 11-60 days after TAI and TAE. Eight were hepatocellular carcinoma and two were metachronous metastatic carcinoma secondary to well-differentiated tubular adenocarcinoma of the stomach and to well-differentiated papillary adenocarcinoma of the sigmoid colon, respectively. Eight patients had liver cirrhosis. No operative mortality occurred. Right lobectomy was performed in four patients, segmentectomy in three, and subsequent segmentectomy in three. All patients were doing well 1-11 mo after surgery. Actuarial survival at 6 mo for these 10 patients was

100%. Five patients experienced complete tumor necrosis and five partial necrosis. Five experienced minimal infarct of the gallbladder, two moderate infarct, and one severe infarct. Hepatic infarct occurred in two cases. TAE plus TAI is justified for treatment of hepatic malignancies in selected cases. (11 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

37. PROGNOSIS IN PATIENTS WITH OBSTRUCTING COLORECTAL CARCINOMA.

Ohman U
Dept. Surgery, Karolinska Hosp., S-104 01 Stockholm, Sweden
Am J Surg; 143(6):742-747 1982

Over a 30 yr interval (1950 to 1979), 1,061 patients with colorectal carcinoma were seen; 148 presented with bowel obstruction and in this retrospective study were compared with those having nonobstructive tumors. The age and sex distribution did not differ between the groups. The curability rate was 53%, versus 72% for nonobstructed patients; the 5 yr survival rate was 16% overall and 31% in curable cases, versus 37 and 50% for elective patients, respectively. Survival within tumor stages did not differ between the groups; the difference in outcome was mainly a result of obstructed patients having fewer Stage A and more Stage C lesions. Most right-sided growths were primarily resected, while the left-sided growths were mainly treated with staged resection. Operative mortality for curable patients was 8%, not different from the 7% rate in elective patients. The 5 yr survival rate was 19% after primary and 35% after staged resection. It was concluded that patients with bowel obstruction secondary to colorectal carcinoma have low curability and survival rates, primarily because of advanced disease at the time of diagnosis and treatment. (Author abstract) (39 Refs)

38. LOCAL RECURRENCES FOLLOWING RECTAL CARCINOMA ETIOLOGY, DIAGNOSIS, PROGNOSIS.

Hermanek P, Gall FP, Altendorf A
Chirurgische Universitatsklinik, Maximiliansplatz, D-8250 Erlangen, W. Germany
Langenbecks Arch Chir; 356(4):289-298 1982

Local recurrences of rectal carcinoma were observed in 167/729 patients within the first 5 yr after surgery. The median lapse between surgery and the diagnosis of recurrence was 11 mo. The recurrences occurred within the first 2 yr in 149/167 patients. The frequency of recurrences was 19.0% for insular tumors and 39.0% for circular ones; 14.4% for tumors up to 30 mm diameter, 22.7% for 31-50 mm and 29.1% for tumors larger than 50 mm; 28.9% for ulcerous tumors; 9.9% in Dukes' Stage A, 25.3% in B and 32.6% in C; 22.2% for adenocarcinomas, 30.3% for mucinous adenocarcinomas and 50% for signet-ring-cell and undifferentiated carcinomas; 19.6% in histological malignancy grade G1, 22.6% in G2 and 28.8% in G3. The incidence of recurrences was 11.7% after rectal resection without local tumor dissemination with aboral safety margins exceeding 30 mm, 17.9% after rectal extirpation without local tumor dissemination (limited surgery), 29.3% after rectal resection without local tumor dissemination (aboral safety margin 11-30 mm), and 37.5% after rectal extirpation or resection with local tumor dissemination or with aboral safety margins smaller than 10 mm. Radical curative reoperations were possible in 33/167 patients, mostly in patients subjected to limited surgery. The overall 5-yr survival rate was 74% for all 729 patients, 12% for those with local recurrences and 33% for the patients amenable for radical reoperation. (22 Refs) (In GER)

39. JUVENILE POLYPS OF THE COLON AND RECTUM.

Mazier WP, MacKeigan JM, Billingham RP, Dignan RD
Ferguson Clinic, Grand Rapids, MI
Surg Gynecol Obstet; 154(6):829-832 1982

Two hundred and fifty-eight patients with juvenile polyps were reviewed. Ten patients less than 20 yr of age were found to have adenomas. The points to be presented can, therefore, be emphasized. Juvenile polyps are a distinct pathologic entity and can occur at any age and in either sex. Adenomas do exist in pediatric patients. We should not assume that every polyp in patients less than 20 yrs of age is automatically a juvenile polyp and therefore, benign. Barium enema is recommended for any child or adolescent in whom one or more polyps are found. In multiple polyposis, the finding that one polyp is of the juvenile type does not necessarily rule out the presence of adenoma. Any patient with a solitary adenoma who has multiple polyps, whether adenoma or juvenile polyps, should be observed at appropriate intervals by sigmoidoscopic, roentgenographic and, possibly, colonoscopic examination. Finally, we hope that this study will inspire others to investigate further this interesting pathologic condition. (Author abstract) (5 Refs)

40. ACUTE APPENDICITIS AS A SIGN OF A COLORECTAL CARCINOMA.

Arnbjornsson E
Dept. Surgery, Univ. Lund, S-221 85 Lund, Sweden
J Surg Oncol; 20(1):17-20 1982

The relationship of acute appendicitis occurring previous to cancer in colon and rectum was studied in the consecutive records of 561 patients, of 40 yr of age and older, operated upon with an appendectomy because of acute appendicitis. Sixteen (2.9%) of these patients were readmitted within 3 yr because of a carcinoma in colon or rectum. The incidence of carcinoma in the colon and rectum in the population, of the same age, is only 0.1%, according to the Swedish Cancer Registry (1). This difference is statistically significant. Where acute appendicitis and colon carcinoma co-exist, the danger is that the carcinoma may be missed. Therefore, any patient over the age of 40 presenting with acute appendicitis should be carefully checked for carcinoma in the colon. (Author abstract) (21 Refs)

41. ANTICOAGULANT-INDUCED HEMORRHAGE REVEALING OCCULT DISEASE. REPORT OF 21 CASES.

Cecchetti G, Lecchi G
Istituto di Clinica Medica III, Universita di Milano, Via Pace, 15, 20122 Milan, Italy
Minerva Med; 73(19):1269-1273 1982

Thirty-eight of 950 patients treated with anticoagulants for various reasons developed major hemorrhages. Bleeding was partially due to previously unknown serious diseases in 21/38 patients, including tumors in 9. The tumors revealed by the hemorrhage included carcinoma of urinary bladder, renal carcinoma, gastric adenocarcinoma, colonic adenocarcinoma, carcinoma of the uterine cervix, papilloma of the renal pelvis, uterine fibromyoma (2 cases) and a pulmonary tumor. (33 Refs) (In ITA)

42. BASALOID TUMOR OF THE SIGMOID COLON.

Hall-Craggs M, Toker C
Dept. Pathology, Univ. Maryland Hosp., 22 South Greene St., Baltimore, MD, 21201
Hum Pathol; 13(5):497-500 1982

A second case of basaloid carcinoma arising in the midsigmoid colon is reported. By light microscopy the tumor was seen to be composed of islands of small, poorly differentiated cells separated by cellular connective tissue. Also seen were small foci of keratinized cells. Ultrastructure study confirms the largely basal character of the tumor and also shows some cells containing tonofilament bundles, representing a more squamoid differentiation. The similarity of this tumor to basaloid tumors arising in the transitional epithelium of the anal canal is discussed, and the suggestion that the tumor arises from a pluripotential basal cells is made. (Author abstract) (10 Refs)

43. MICROSCOPIC INTRAEPITHELIAL NEOPLASIA IN LARGE BOWEL MUCOSA.

Shamsuddin AM
Dept. Pathology, Univ. Maryland Sch. Medicine, 10 South Pine St., Baltimore, MD, 21201
Hum Pathol; 13(5):510-512 1982

Early neoplastic changes within the nonpolypoid mucosa of the large bowel have been incidentally discovered in two individuals. One these patients is a 31-yr-old man without any known large bowel disease; the other is a 61-yr-old woman with diverticulosis. Only small microscopic foci of several neoplastic crypts were observed in otherwise normal-appearing mucosa. This finding lends support to the concept that cells in the crypts, irrespective of their location either in the flat mucosa, polyps, diverticula, or elsewhere, are susceptible to neoplastic transformation. (Author abstract) (24 Refs)

44. MULTICENTRIC MALIGNANT FIBROUS HISTIOCYTOMAS OF THE COLON. REPORT OF A CASE AND REVIEW OF THE SUBJECT.

Levinson MM, Tsang D
Dept. Surgery, Univ. Arizona Health Sciences Center, 1501 N. Campbell, Tucson, AZ, 85719
Dis Colon Rectum; 25(4):327-331 1982

Malignant fibrous histiocytoma is a primitive mesenchymal tumor usually found in the soft tissues of the extremity or torso of adults. Only two previous reports of this lesion in the abdominal viscera are present in the world medical literature. A case is reported of three synchronous tumors in the rectum, colon, and omentum with the pathologic appearance of malignant fibrous histiocytoma. Although resected completely with a transverse colocolostomy and a low-anterior resection, the expected behavior of this tumor is one of aggressive local recurrence followed by distant metastasis. The clinical and pathologic characteristics of malignant fibrous histiocytoma are reviewed. (Author abstract) (13 Refs)

45. COLONIC LYMPHOMA PRODUCING ALPHA-CHAIN DISEASE PROTEIN.

Cho C, Linscheer WG, Bell R, Smith R
Veterans Admin. Medical Center, Syracuse, NY, 13210
Gastroenterology; 83(1):121-126 1982

A case of a 57-yr-old man of German and English descent who was admitted to hospital for evaluation of melena and hematemesis and presented colonic lymphoma without malabsorption is reported . Alpha-chain disease protein was demonstrated in tumor tissue, in serum, and in urine. The tumor in the colon was surgically removed and diagnosed as a malignant lymphoma of lymphocytic type. Tumor tissue infiltrated in the mesentery could not be excised. (23 Refs)

46. BLUE RUBBER-BLEB NEVUS SYNDROME.

Wong SH, Lau WY
Government Surgical Unit, Queen Mary Hosp., Pokfulam Road, Hong Kong, Hong Kong
Dis Colon Rectum; 25(4):371-374 1982

A 22-yr-old man with blue rubber-bleb syndrome is reported on. This is a rare syndrome. This patient is of particular interest because he had a combination of rare features: (1) five ileoileal intussusceptions each with a hemangioma acting as the lead point, were present during operation; (2) there was an angiomatous lesion of the glans penis; (3) this is the first case reported in a Chinese person. An aggressive surgical approach was used with success. Preoperative and perioperative investigations, including operative colonoscopy, were used to localize the gastrointestinal hemangiomas. (Author abstract) (17 Refs)

47. CARCINOMA OF THE SIGMOID: A COMPLICATION OF URETEROSIGMOIDOSTOMY.

Charron J, Delisle R
Ste. 601, 1851 Sherbrooke St. E, Montreal, PQ H2K 4L5, Canada
Can J Surg; 25(3):253-257 1982

The case of a 58-yr-old man who had carcinomatous change in the sigmoid colon many yr after ureterosigmoidostomy prompted the authors to review the French and English literature on the subject. They found 47 cases in addition to their own, and noted a dramatic increase in the last 10 yr, even though ureterosigmoidostomy is now seldom used. The latency of this complication makes it pertinent today. In the hope of determining the etiology of the complication, the authors studied the relation between the initial lesion for which the diversion was carried out and the nature of the colonic tumor that ensued, and have attempted to draw some conclusions. None of the current theories of pathogenesis seem satisfactory. By underlining the early clinical manifestations, the authors attempt to promote earlier diagnosis and better chances of survival for patients with carcinoma of the colon after ureterosigmoidostomy. (Author abstract) (36 Refs)

48. COMBINATIONS OF 5-FU, HYPOXANTHINE, AND ALLOPURINOL IN CHEMOTHERAPY FOR HUMAN COLON ADENOCARCINOMA XENOGRAFTS.

Houghton JA, Houghton PJ
Div. Biochemical and Clinical Pharmacology, St. Jude Children's Res. Hosp., P.O. Box 318, 332 N. Lauderdale, Memphis, TN, 38101
Cancer Treat Rep; 66(5):1201-1206 1982

A series of four human colon adenocarcinomas, growing as xenografts in immune-deprived mice, have been used to evaluate the efficacy of 5-FU in combination with two purines, hypoxanthine (Hx) and allopurinol (HPP), which have reduced the toxicity of 5-FU in host mice. Tumor-bearing mice were treated at 7-day intervals with 5-FU administered simultaneously with the protecting agents (Hx and HPP). Two tumor lines (HxVRC5 and HxGC3), insensitive to 5-FU alone, failed to show any response to this combination. In 5-FU-sensitive HxELC2 tumors, the combination of 5-FU with Hx and HPP did not increase the therapeutic index, and in HxHC1 xenografts, antagonism to 5-FU cytotoxicity was observed. Tumor response in relation to the pathways of 5-FU metabolism is discussed. (Author abstract) (19 Refs)

49. DIFFERENTIAL RESPONSES TO X-IRRADIATION OF SUBPOPULATIONS OF TWO HETEROGENEOUS HUMAN CARCINOMAS IN VITRO.

Leith JT, Dexter DL, DeWyngaert JK, Zeman EM, Chu MY, Calabresi P, Glicksman AS
Box G, Brown Univ., Providence, RI, 02912
Cancer Res; 42(7):2556-2561 1982

The responses of two heterogeneous human cancer cell lines and their derivative clones to graded single doses of x-rays were examined in vitro. One system consisted of the human colon carcinoma line DLD-1 and two subpopulations (clones A and D). The second system consisted of the human lung carcinoma line (LX1) and four subpopulations (LX1-1, LX1-2, LX1-3 and LX1-9). These subpopulations have previously been shown to be markedly heterogeneous in terms of such characteristics as karyotype, morphology, drug sensitivity, tumorigenicity, and expression of membrane glycoproteins (such as carcinoembryonic antigen and tumor colonic mucoprotein antigen). Exponentially growing cultures were irradiated with graded single doses of 100-kVp x-rays. Survival was assessed using colony formation as the end point, and responses from multiple experiments were fitted to the single-hit, multitarget equation of cell survival. Values for the mean lethal dose (Do, grays), quasithreshold dose (Dq, grays), and extrapolation number (n) were obtained. For the human colon adenocarcinoma system, these values for the three tumor lines were: DLD-1, 0.95, 2.34, and 11.7; clone A, 1.06, 2.23, and 8.20; and clone D, 1.08, 1.89, and 5.80. For the human lung carcinoma system, these values for the five sublines were: LX1, 1.14, 0.19, and 1.20; LX1-1, 0.96, 2.06, and 8.54; LX1-2, 0.96, 0.88, and 2.48; LX1-3, 0.68, 2.05, and 20.3; and LX1-9, 1.12, 0.00, and 1.00. These two human tumor systems therefore exhibit variability in their intrinsic sensitivity to x-irradiation. The data indicate that failure of some human carcinomas to respond to physical treatment modalities can be due to preexisting resistant subpopulations. (Author abstract) (43 Refs)

50. CALORIE RESTRICTION: EFFECT ON GROWTH OF HUMAN TUMORS HETEROTRANSPLANTED IN NUDE MICE.

Giovanella BC, Shepard RC, Stehlin JS, Venditti JM, Abbott BJ
Stehlin Foundation for Cancer Res., 777 St. Joseph Professional Building, Houston, TX, 77002
JNCI; 68(2):249-257 1982

The presence of four human malignant tumors (1 breast, 1 lung, and 2 colon carcinomas) growing sc as heterotransplants in nude mice did not significantly affect the body wt of adult animals until the tumors reached very large dimensions (tumor wt greater than 15% of the body wt). However, a colon carcinoma (HT 29) induced a cessation of the natural rate of body wt increase when it grew in young adults (animals weighing approx 25 g which will gain 6 g or approx 25% body wt in 1 mo). Calorie restriction at all the levels tested (8, 6, 4, and 2 g/day/mouse) with standard pelletized mouse food produced both wt loss in the animals (with and without tumor) and a lowering of the growth rate of all the four tumors tested growing at a sc site and/or under the kidney capsule. Each tumor responded differently to calorie restriction. The four tumors tested grew equally in both male and female nude mice. Young animals weighing 20 g inoculated with a fifth tumor (MeWo melanoma) exhibited tumor growth inhibition proportional to restriction of calorie intake. Their survival, however, did not improve. (Author abstract) (41 Refs)

51. EVIDENCE OF A PHOSPHORYLATED PROTEIN SPECIFIC OF HUMAN COLON CARCINOMA CELLS.

Munsch N, Raux H, Fondaneche MC, Burtin P
Inst. de Recherches Scientifiques sur le Cancer, B.P. 8, 94802 Villejuif Cedex, France
Biochem Biophys Res Commun; 106(1):87-93 1982

Two human tumor cell lines, HT29 and Caco2, and the mammary tumor cell line MDA -MB-231 synthesize in culture a 42 kilodalton (42K) protein detectable by immunoprecipitation. This protein, which is phosphorylated in the two colon tumor cell lines, is not detectable by antisera against normal adult colon, suggesting that the 42K protein represents a tumor specific antigen. Addition of a differentiating agent, retinoic acid, reduces the growth of the tumor cells by 50%, but has no effect on the expression of the 42K protein. (10 Refs)

52. THE ASSESSMENT OF RESPONSE OF MURINE TRANSPLANTABLE COLON TUMORS TO COMBINATION CHEMOTHERAPY.

Cowen DM, Siegerstetter J, Janik AC, Double JA
Unit Cancer Res., Medical Sch., Univ. Leeds, Leeds, England
J Cancer Res Clin Oncol; 103(2):119-126 1982

The mouse adenocarcinoma of the colon (MAC) system, which has been shown to be a good model for human colorectal carcinoma in terms of its chemosensitivity was tested with two modified human protocols, semustine + 5-fluorouracil (MeCCNU + 5 FU) and carmustine (BCNU) + 5 FU in an attempt to evaluate its suitability as a model for developing new regimens of combination chemotherapy for treating patients with colorectal carcinoma. This attempted evaluation raised problems regarding, firstly, the length of time available before tumors became too large in control and non-responding hosts to maintain adequate mobility and, secondly, the assessment of response to the drugs. The commencement of drug administration 3 days after transplantation and the assessment of response by measuring delay in time for tumor growth to reach a given volume, with the results analyzed by Gehan's (generalized Wilcoxon) test, gave a workable method of evaluation. This method is presented as being suitable for use in the study of transplantable solid tumor lines as models for combination chemotherapy. (Author abstract) (9 Refs)

53. RESPONSE OF TRANSPLANTABLE TUMORS OF MICE TO ANTHRACENEDIONE DERIVATIVES ALONE AND IN COMBINATION WITH CLINICALLY USEFUL AGENTS.

Corbett TH, Roberts BJ, Trader MW, Laster WR, Griswold DP, Schabel FM
Southern Res. Inst., P.O. Box 3307-A, 2000 9th Ave. S., 2000 9th Ave. S., Birmingham, AL, 35255
Cancer Treat Rep; 66(5):1187-1200 1982

Other investigators have demonstrated that dihydroxyanthracenedione (DiOHA) and anthracenedione acetate (AA) are active against a broad spectrum of transplantable mouse tumors. DiOHA and AA are in clinical trial in the US; AA is in clinical trial in Europe. Because of the broad spectrum of activity of these DNA binders against murine tumors and due to their promising clinical utility, we have evaluated these agents in combination with a variety of clinically useful antitumor drugs. Studies were carried out against three colon adenocarcinomas (38, 06/A, and 11/A), three mammary adenocarcinomas (13/C, 16/C, and 14), and two lymphocytic leukemias (P388 and L1210). The therapeutic synergism of one of these combinations, DiOHA and cisplatin, has been previously reported. Four additional combinations which were found to have confirmed therapeutic synergism are reported here: DiOHA and palmO-ara-C, DiOHA or AA and 5-fluorouracil, DiOHA or AA and vincristine, and DiOHA and dacarbazine. The combination toxicity indices (CTI; a measure of the degree of overlap in dose-limiting toxic effects) were obtained for all the following combinations: DiOHA and palmO-ara-C = 1.25-1.6; DiOHA or AA and 5-FU = 1.2-1.3; DiOHA or AA and vincristine = 1.6; and DiOHA and dacarbazine = 1.3-1.5. A CTI of 1.0 indicates complete overlap in dose-limiting toxic effects, eg, only 50% of the maximum tolerated dose of each agent can be used in combination. On the other hand, a CTI of 2.0 indicates no overlap in toxicity, and 100% of the maximum tolerated dose of each agent can be used in combination. (Author abstract) (17 Refs)

54. KINETIC PROPERTIES OF THYMIDINE KINASE FROM THE CYTOSOL OF A RAT COLON ADENOCARCINOMA.

Kowal EP, Markus G
Dept. Experimental Therapeutics, Roswell Park Memorial Inst., Buffalo, NY, 14263
J Med; 13(1/2):97-120 1982

Thymidine kinase (EC 2.7.1.75) from the cytosol of a rat colon adenocarcinoma was partially purified by affinity chromatography, and the kinetic properties of this enzyme were investigated. The initial velocity was analyzed as a function of the concentrations of thymidine and Mg-ATP complex; The latter concentration was calculated using the association constant for the complex, which was experimentally determined under the approx reaction conditions for the kinase. Normal Michaelis-Menten kinetics were observed, except for substrate inhibition at high Mg-ATP concentrations. The Km for thymidine was 2.5 uM, that for Mg-ATP was 7.3 uM. An intersecting pattern of straight lines was observed for the Lineweaver-Burk plot for each substrate in the presence of different constant concentrations of the other, indicating a sequential mechanism. Product inhibition studies revealed that a random addition sequential mechanism was the case. It was also found by kinetic analysis that free ATP, followed by Mg++ ion could add to the enzyme in place of Mg-ATP in the kinetic mechanism; binding of Mg++ ion first, followed by ATP did not occur. Mg-dTTP, an inhibitor of thymidine kinase, converted the normally straight Lineweaver-Burk plot for Mg-ATP to concave upward, indicating a sigmoidal saturation curve. The inhibition curve for Mg-dTTP at saturating concentrations of substrates was also sigmoidal. Such data are consistent with the hypothesis that Mg-dTTP is an allosteric inhibitor of thymidine kinase. (Author abstract) (39 Refs)

55. LYMPHOBLAST TRANSFORMATION FOLLOWING ADJUVANT TREATMENT OF AN INDUCED COLONIC CANCER WITH LEVAMISOLE AND FLUOROURACIL.

Windle R, Bell PR
Dept. Surgery, Univ. Leicester, Clinical Sciences Buliding, Royal Infirmary, P.O. Box 65, Leicester LE2 7LX, England
Cancer Immunol Immunother; 12(3):267-271 1982

Effects of levamisole (LV) and fluorouracil (5FU) on lymphoblast transformation (LT) were studied in the dimethylhydrazine (DMH)-induced colonic cancer model in Sprague-Dawley rats to determine the optimum schedule for administration of LV and 5FU following surgery for colorectal cancer. The median counts/min obtained prior to surgery in 90 normal animals was 52,229 (range 12,307-226,949) and that in DMH-treated animals was 27,407 (range 1,056-79,497). The mean lymphocyte counts for each treatment group are tabulated. No significant change following surgery was observed in any group. Considering the groups of rats given neither chemotherapy nor immunotherapy, LT was depressed on the first postoperative day in both groups. However, depression was greater in the DMH group than in normal animals. The administration of LV prevented the depression of LT on the first postoperative day when given both before and after surgery. When LV was given only after surgery, LT was restored to pre-operative levels in both groups of animals at day 3. 5FU did not significantly affect the depression of LT after surgery alone in the DMH group but produced a return of LT to pre-operative levels at day 3 in the normal animals. In the DMH animals a combination of 5FU and LV led to a greater depression of LT on the first postoperative day than following no treatment or LV alone. At day 3 LT was greater than on day 1, but the degree of depression was still greater than that following LV alone. At day 7 LT still had not returned to pre-operative levels. If LV was given 1 day after 5FU the depression of LT was corrected by day 3 but the level was not maintained at day 7. No significant prolongation of survival was observed in any of the treated groups compared with untreated controls. (20 Refs)

56. INTESTINAL ADAPTATION AND EXPERIMENTAL CARCINOGENESIS AFTER PARTIAL COLECTOMY. INCREASED TUMOUR YIELDS ARE CONFINED TO THE ANASTOMOSIS.

Williamson RC, Davies PW, Bristol JB, Wells M

Univ. Dept. Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, England

Gut; 23(4):316-325 1982

Small-bowel resection enhances experimental colorectal carcinogenesis, probably by stimulating epithelial cell proliferation. The possibility that similar mechanisms might explain metachronous large-bowel cancers in man was tested in Sprague-Dawley rats submitted to partial colectomy before or after a 5-wk course of azoxymethane (total dose 50 mg/kg). The timing of operation did not affect tumor yields at 40 wk. Cecal resection augmented mucosal mass in the ileum and right colon but did not affect carcinogenesis. Right hemicolectomy only increased ileal segmental wt (by 22%); left hemicolectomy increased the protein and DNA contents of the residual right colon by 18-42%. Large-bowel tumors in 84 rats were distributed as follows: proximal colon 36, colonic anastomosis 51, distal colon 87, rectum 43. Consistent with this left-sided predominance, left hemicolectomy reduced the number of large-bowel tumors. A twofold increase in distal tumors after both transection and right hemicolectomy simply reflected the high incidence of anastomotic tumors. Furthermore, one rat given vehicle as opposed to carcinogen developed an invasive mucinous adenocarcinoma at the colorectal anastomosis, after left hemicolectomy. The large bowel shows limited adaptation to partial resection and is not at increased risk of carcinogenesis, except in the region of the suture line. (Author abstract) (48 Refs)

57. INTERFERENCE WITH DIMETHYLHYDRAZINE INDUCTION OF COLON TUMORS IN MICE BY EPSILON-AMINOCAPROIC ACID.

Corasanti JG, Hobika GH, Markus G
Dept. Experimental Biology, Roswell Park Memorial Inst., New York State Dept. Health, Buffalo, NY, 14263
Science; 216(4549):1020-1021 1982

The antifibrinolytic agent epsilon-aminocaproic acid given in the drinking water to Swiss ICR/Ha mice significantly counteracted the appearance of colorectal tumors induced by 21 weekly injections of 1,2-dimethylhydrazine. The drug affected both the number and the location of the tumors and, in some animals, altogether prevented their appearance. The low concentrations of epsilon-aminocaproic acid in the plasma of four control mice given the agent labeled with carbon-14 for 3 days suggest that the effect may depend not on inhibition of plasminogen activator activity, but on interference with the binding of some substance to the strong lysine binding site of plasminogen. (Author abstract) (29 Refs)

58. DIMETHYLHYDRAZINE-INDUCED COLONIC NEOPLASIA: DISSOCIATION FROM ENDOGENOUS GASTRIN LEVELS.

Oscarson JE, Veen HF, Ross JS, Malt RA
(c/o Malt) Massachusetts General Hosp., Boston, MA, 02114
Surgery; 91(5):525-530 1982

The potential tropic effect of gastrin in promoting colonic carcinogenesis was tested in rats (n = 133) with 6-to 16-fold variations in endogenous gastrin resulting from antrectomy or fundectomy, followed by 12 injections of 1,2-dimethylhydrazine (10 mg/kg). The incidence and grade of differentiation of resulting tumors, as well as the thickness, content of nucleic acids, and specific activity of DNA in colonic mucosa, were similar in both high-gastrin and low-gastrin animals and were unchanged from data in unoperated control animals receiving only the carcinogen. Long-term changes in endogenous gastrin concentration are not followed by colonic mucosal tropic effects, and gastrin does not act as a cofactor in dimethylhydrazine-induced carcinogenesis at this dosage. (Author abstract) (25 Refs)

59. DETECTION OF CARCINOGENIC EXPOSURES BY URINALYSIS: INDUCTION OF CELL-MEDIATED IMMUNITY.

Stevens RH, Cole DA
Radiation Res. Lab., Dept. Radiology, Univ. Iowa, Iowa City, IA, 52242
Toxicol Lett; 11(3/4):299-303 1982

The colon carcinogen 1,2,-dimethylhydrazine (DMH: 0.1 to greater than 10 mg/kg) was administered sc to male Fisher F344 inbred rats; urine was collected over a 24 hr period and injected ip into a group of normal unexposed rats. DMH and its metabolites were excreted within 15 min in the urine and nearly 65% metabolized over a 24-hr interval. Cell mediated immunity (CMI) was measured by killing/injury of cultured x-ray induced rat small bowel adenocarcinoma target cells by peripheral blood lymphoid cells of urine-exposed animals. CMI was increased by urine collected from DMH exposed rats; a dose-response curve relationship was found, suggesting the presence of mutagenic/carcinogenic components. Although the actual DMH concentration in the urine was not known, it was less than 10(-4) times LD50 (1 g/kg) and 10(-3) times the amount necessary for tumor induction over a 20-mo latency period. This method has potential as a rapid non-invasive technique for screening individuals exposed to carcinogens. (15 Refs)

60. PATHOGENESIS OF 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOMAS IN RAT INTESTINE. 1. THE INDUCTION OF MUCIN PRODUCING CARCINOMAS IN RAT INTESTINE.

Takemiya M, Miyayama H, Takeuchi T

Dept. Pathology, Kumamoto Univ. Sch. Medicine, 2-2-1 Honjo, Kumamoto 860, Japan

Acta Pathol Jpn; 32(2):257-264 1982

Seventy four white male Wistar rats were divided into two groups and given weekly subcutaneous injections of 30 mg 1,2-dimethylhydrazine (DMH) 2HCl/kg body weight for 10 or 15 weeks, respectively, and the histological properties and distribution of DMH-induced rat carcinomas were investigated. The carcinomas induced by DMH were classified mainly into mucin producing carcinomas and non-mucin producing ones. In the large intestine, the group treated for 15 weeks induced significant incidences of mucin producing carcinomas composed mainly of cells containing intracellular mucin. Mucin producing carcinomas consisted of poorly differentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma, and these often coexisted within the same tumor mass. Mucin producing carcinomas tended to develop in the proximal colon and cecum, while non-mucin producing carcinomas were frequent in the distal colon. This method was thought to be a useful model to study glycoproteins of cancer cells. (Author abstract) (17 Refs)

61. EXPERIMENTAL COLORECTAL CARCINOGENESIS.

Martin MS

Laboratoire d'Immunologie, Faculte de Medecine, 7, boulevard Janne-d'Arc, F-21033 Dijon, France

Gastroenterol Clin Biol; 6(4):382-391 1982

Multiple intestinal tumors have successfully been induced in rats following 6 mo of subcutaneous injection with 1,2-dimethylhydrazine (DMH). The specificity of DMH depends to a large extent on the mode of administration, and the dose modifies the distribution of the lesions. DHM induces more intestinal tumors at low doses than some of the other compounds used for carcinogenic purposes. Age of the animal has an effect on the specificity of the action of carcinogens. Sex of the animal is also a factor in intestinal carcinogenesis. Intestinal tumors induced by DMH appear more rapidly in males than in females who seem less susceptible to colorectal cancers. The most frequently induced tumors are adenocarcinomas which occurs most often in the distal half of the colon. Mucous secreting carcinomas which predominate in the proximal part of the colon are less commonly encountered. Adenomas are observed much more commonly in the mouse than in the rat and they resemble the human adenomas. Like human colon cancers, experimental cancers of the colon can produce more or less specific antigens. The morphological transformation of the colons epithelial cells is accompanied by biochemical alterations and complex interactions affecting nutrition, intestinal flora, biliary acids, and immune defenses. Animal models are necessary to study the complicated assortment of factors in human colon cancer. (107 Refs) (In FRE)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

62. LEWIS BLOOD-TYPE MAY AFFECT THE INCIDENCE OF GASTROINTESTINAL CANCER.

Koprowski H, Blaszczyk M, Steplewski Z, Brockhaus M, Magnani J, Ginsburg V
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Lancet; 1(8285):1332-1333 1982

The frequency of gastrointestinal cancer antigen (GICA) was studied in the sera of 315 patients with gastrointestinal cancer (GIC), of 89 patients with other malignancies, and of 108 healthy subjects, and on tumor cells from some of the GIC patients. Sera of 64% of the patients with clinically and histologically proven colorectal cancer, 92% of patients with pancreatic cancer, and 72% of patients with gastric cancer inhibited binding of anti-GICA monoclonal antibody to GICA-containing cancer cells. Sera of 8% of patients with malignancies other than GIC and 2% of healthy subjects inhibited binding. Among the eight patients with tumors other than GIC whose sera inhibited binding of the antibody, three had liver carcinoma. GICA was expressed in 55% of the colorectal cancer tissue samples, in 82% of pancreatic cancer tissues, and in 100% of gastric cancer tissues. Cells of 1/8 liver carcinomas and 1/5 gallbladder carcinomas were positive for GICA. The relationship of Lewis blood type to GIC and GICA expression is discussed. (14 Refs)

63. ATHEROSCLEROSIS AND POLYPS OF THE COLON. QUANTIFICATION OF PRECURSORS OF CORONARY HEART DISEASE AND COLON CANCER.

Correa P, Strong JP, Johnson WD, Pizzolato P, Haenszel W
Dept. Pathology and Biometry, Louisiana State Univ. Medical Center, 1542 Tulane Ave., New Orleans, LA, 70012
J Chronic Dis; 35(5):313-320 1982

The prevalence of adenomatous and hyperplastic polyps of the colon and the degree of involvement of the aorta by atherosclerotic lesions were evaluated in 842 autopsies from New Orleans. A positive statistical association between the two variables was found in white males under 75 yr of age. In black males a positive correlation between atherosclerotic lesions and adenomatous (but not hyperplastic) polyps was found. The most extensive involvement of the aorta by atherosclerosis was found in patients in whom adenomatous and hyperplastic polyps coincided. The possibilities that dietary factors may account for these findings and its relevance in relation to colon cancer and coronary heart disease are discussed. (Author abstract) (31 Refs)

64. HEREDITARY ADENOMATOSIS OF THE COLON AND RECTUM: RELEVANCE TO CANCER PROMOTION AND CANCER CONTROL IN HUMANS.

Kopelovich L
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Genet Cytogenet; 5(4):333-351 1982

Means of detecting persons at risk for colorectal cancers are described. SF cells, derived from normal-appearing biopsies of ACR gene carriers, appear to exist in an initiated state as the result of a dominant mutation. Topics discussed in relation to ACR and SF cells and colorectal neoplasms include the following: membrane-associated parameters, metabolic alterations, differential susceptiblity to transformation by chemical and physical agents and oncogenic viruses, cancer-related antigens, tissue culture studies, tumor promotion, genetic mechanisms, and cancer prognosis and control. (141 Refs)

65. PEROXIDASE LEVELS IN FOOD: RELEVANCE TO COLORECTAL CANCER SCREENING.

Caligiore P, Macrae FA, StJohn DJ, Rayner LJ, Legge JW
(c/o St. John) Dept. Gastroenterology, Royal Melbourne Hosp., RMH Post Office, Victoria 3050, Australia
Am J Clin Nutr; 35(6):1487-1489 1982

The peroxidase content of aqueous extracts of a variety of fresh foods was measured by spectrophotometry and expressed in relation to the pseudoperoxidase activity of blood. A wide range of activities was found in extracts from different foods but inter-sample and inter-seasonal variation from any single food was of no practical significance. The results may be used to design diets suitable for colorectal cancer screening programs that use peroxidase-dependent fecal occult blood tests. (Author abstract) (14 Refs)

66. SOCIO-ECONOMIC CLASS DIFFERENCES IN CANCER INCIDENCE IN CALI, COLOMBIA.

Cuello C, Correa P, Haenszel W
Dept. Pathology, Faculty Medicine, Universidad del Valle Cali, Cali, Colombia
Int J Cancer; 29(6):637-643 1982

Based on census tract information, cancer incidence rates for three socioeconomic strata of the city of Cali, Colombia, were calculated. Strong negative associations with socioeconomic status were found for cancers of the cervix and stomach. Colon cancer and endocrine-related cancers were positively associated with socioeconomic status, while no such association was found for rectal cancer. Contrary to data from developed countries, all smoking-related cancers were positively associated with socioeconomic class. The role of socio-economic gradients in developing countries is stressed as a basis for etiological research. (Author abstract) (30 Refs)

67. THE COSTS AND EFFECTS OF SCREENING FOR CANCER AMONG ASBESTOS-EXPOSED WORKERS.

McNeil BJ, Eddy DM
Dept. Radiology, Harvard Medical Sch., 25 Shattuck St., Boston, MA
J Chronic Dis; 35(5):351-358 1982

Several million workers previously exposed to asbestos are at risk each year for developing asbestosis or cancer as a result of this exposure. We have reviewed the data on the general effectiveness of screening for the two most common cancers found in these workers (lung cancer and colo-rectal cancer) and have compared the relative benefits expected from screening workers for colon or lung cancer 10, 15, 20 or 25 yr after their initial exposure. Although lung cancer is common, there is little evidence at present that screening for this disease is effective in reducing mortality. Colon cancer is less common, there is more evidence that screening is effective, and the relatively high risk of dying from this disease in asbestos workers makes screening useful. The cost per additional year of life extended by screening is only a few hundreds of dollars, making colon cancer screening programs for asbestos workers considerably more cost-effective than most other screening programs. We conclude that occupational safety agencies should consider implementing screening programs for colon cancer in workers exposed to asbestos over 10 yr ago. (Author abstract) (34 Refs)

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. RESULTS OF A SCREENING FOR COLORECTAL CARCINOMA. A FIELD-TRIAL IN THE TOWN MOLLN.

Kruse JU, Jacobi D, Muller-Wieland K
(c/o Muller-Wieland), Medizinische Universitatsklinik Hamburg-Eppendorf, Martinistrasse 52, D-2000 Hamburg 20, W. Germany
Z Gastroenterol; 20(5):273-275 1982

A screening test for colorectal disease was conducted among residents and visitors in the town of Molln. Histories and fecal samples for occult blood tests (FEC) were received from 3,627 residents over 40 yr old (Group A). Participation in the survey was 42.1% for men and 42.0% for women. An additional 1116 responses were obtained from residents under 40 yr old and visitors (Group B). Participation by this group was 19%. Positive FEC results were obtained for 127 persons in Group A and 49 in Group B. Individuals with positive FEC or anamnestic evidence of colorectal disease were referred to their personal physicians for rectal palpation, proctoscopy, rectosigmoidoscopy, radiological double-contrast studies, and/or high coloscopy. Among FEC-positive persons 15 carcinomas and 68 ad-

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enomas were detected in 42. Tumors were thus detected in 34.4% of FEC-positive persons and 0.89% of all participants. Hemorrhoids were the most frequent findings with 39.3% of those studied. Among 645 persons with positive anamnestic findings, further diagnostic procedures were performed on 143. Twelve adenomas were found in seven persons; no carcinomas were found in this group. Lack of participation in the study by greater than 50% of those who were sent test materials and questionnaires indicates the need for motivation of the general population to preventive care measures. (3 Refs) (In GER)

2. A PROSPECTIVE STUDY OF DIAGNOSTIC METHODS IN ADENOMA FOLLOW-UP.

Williams CB, Macrae FA, Bartram CI
Div. Gastroenterology, St. Mark's Hosp., City Road, GB-London ECLV 2 PS, England
Endoscopy; 14(3):74-78 1982

Three hundred and thirty patients having had previous colonoscopic polypectomy of adenomas were recalled for follow-up and submitted to all available diagnostic methods: occult blood testing, digital examination, rigid proctosigmoidoscopy, fiber-optic sigmoidoscopy, total colonoscopy and double contrast barium enema. Polyps up to 7 mm diameter were electrocoagulated during diagnostic endoscopy but larger polyps were left in situ for barium enema before polypectomy at a later date. Disparities between endoscopy and x-ray were rechecked by one or both procedures. Occult blood testing, digital examination and rigid proctosigmoidoscopy were found to be inaccurate or ineffective in diagnosis of the 37% of patients with further adenomas or carcinomas. Double contrast barium enema demonstrated 71% of larger lesions compared to the 92% shown by colonoscopy. The commonest sites of x-ray inaccuracy were in the sigmoid colon and cecum. Colonoscopy permits immediate electrocoagulation or snare polypectomy of any lesions seen, as well as being the more accurate investigation and is, therefore, the procedure of choice in post polypectomy follow-up. The mean time taken for diagnostic total colonoscopy in this series was 15.3 min, comparable to the time taken for barium enema. Postal questionnaire showed both procedures to be equally well tolerated by the patients. Thirty percent of colonoscopies were, however, considered technically difficult by the endoscopist, and for these patients it is suggested that follow-up should be by the combination of fibersigmoidoscopy using carbon dioxide insufflation and immediate double contrast barium enema. Should this combination indicate a need for total colonoscopy, then almost all adenomas and cancers would be detected. Total examination of the colon by one or other means is essential, over half the patients with adenomas and three of the five patients with carcinoma showing no pathology in the territory of fibersigmoidoscopy or limited colonoscopy. (Author abstract) (19 Refs)

3. SURVEILLANCE INTERVALS AFTER COLONOSCOPIC POLYPECTOMY.

Waye JD, Braunfeld S
Div. Gastroenterology, Mount Sinai Hosp., New York, NY
Endoscopy; 14(3):79-81 1982

Two hundred twenty-seven patients had multiple follow-up total colonoscopies after initial endoscopic polypectomy. All adenomas were removed at the initial examination ('clean colon') in those patients who had no history of colon cancer, inflammatory bowel disease or polyposis coli; when re-endoscoped within 1 yr 56% of them were found to have further adenomas. Nine percent had adenomas over 10 mm diameter which are presumed to have been missed during the index colonoscopy. Patients with single or multiple adenomas had an equal likelihood of being found to have further lesions on a 1-year follow-up colonoscopy. With an apparent chance of missing a significant-size polyp at colonoscopy of at least 10% we recommend that all patients have a follow-up colonoscopy within 1 year after polypectomy. One hundred thirty three patients in whom no adenomas were found at the 1 yr colonoscopy ('negative colonoscopy') were followed up. The incidence of new adenoma occurring within 4 yr of 'negative colonoscopy' was 35% for those with a single adenoma at the index examination and twice as high for patients with multiple adenomas. If no polyp is found at 1 yr, we recommend that interval follow-up colonoscopies should be performed every 2 yr if more than one adenoma was removed during the initial examination, and every 3 yr if only one was removed. (Author abstract) (12 Refs)

4. CLINICO-RADIOGRAPHIC DIAGNOSIS OF RECURRENCES OF RECTAL CANCER.

Vladimirov VA, Ostapenko TA, Pedchenko KIa
Res. Roentgenoradiological and Oncological Inst., Kiev, USSR
Khirurgiia (Mosk); (5):62-65 1982

Ninety-seven patients (40 men, 57 women; 25-76 yr old) with recurrences of rectal cancer after radical surgery are reviewed. Of 97 patients, 61 had intraintestinal recurrences (43/61 had recurrences in the region of the anastomosis) and 36 had extraintestinal recurrences (21/36 had recurrences in the small pelvis). Radical surgery of the primary tumor included intraabdominal resection (15), abdominal-anal resection (31), Hartmann's operation (11), abdominal-perineal extirpation (31), and transrectal excision (4). Majority of the patients subjected to sphincter-saving surgery developed intraintestinal recurrences (83.6%), while extraintestinal recurrences were dominant in the patients subjected to extirpation of the rectum (87.1%). Of 97 patients, 73 developed recurrence within the first 2 yr after the surgery. X-ray symptoms of recurrence were asymmetrical stenosis of the rectum, irregular contour, and rigidity of the wall. (15 Refs) (In RUS)

5. COLONIC POLYPS IN PATIENTS WITH ACROMEGALY.

Klein I, Parveen G, Gavaler JS, Vanthiel DH
Univ. Pittsburgh Sch. Medicine, 961 Scaife Hall, Pittsburgh, PA, 15261
Ann Intern Med; 97(1):27-30 1982

Seventeen patients with acromegaly were prospectively studied with barium enemas and colonoscopy to investigate the possibility that acromegaly is associated with an increased frequency of colonic polyps and colon cancer. Polyps were identified in nine patients and were removed and examined in eight. In five patients the polyps were adenomatous, and in four of the five there were multiple polyps. The presence of polyps closely correlated with the presence of skin tags ($p = 0.041$) and also with the age of the patient (p less than 0.01). No new cases of colonic cancer were discovered; however, reviewing the records of 44 patients with acromegaly, four cases were previously diagnosed with colon carcinoma. This study identifies a unique group of patients that are at risk for the development of colonic polyps and perhaps colon cancer. (Author abstract) (20 Refs)

6. MORPHOLOGICAL FEATURES OF RECTAL ADENOCARCINOMA FOLLOWING IRRADIATION FROM 25 MEV BETATRON.

Torgushina NS, Iakhontov NE, Obukhova SO
Medical Inst., Gorky, USSR
Vopr Onkol; 28(4):25-29 1982

The effect of brehmstrahlung irradiation from a 25 MEV betatron on rectal adenocarcinoma was studied in 34 patients in comparison with control material from 61 patients. It was found that pronounced changes in tumor tissue are caused by such preoperative treatment: tumor is reduced in size, DNA synthesis and mitotic activity are suppressed considerably and pathological mitoses increase. Morphological observations show that rectal adenocarcinoma is markedly susceptible to brehmstrahlung irradiation from a 25 MEV betatron. (Author abstract) (10 Refs) (In RUS)

7. DNA DISTRIBUTION IN HUMAN COLON CARCINOMAS AND ITS RELATIONSHIP TO CLINICAL BEHAVIOR.

Wolley RC, Schreiber K, Koss LG, Karas M, Sherman A
(c/o Koss), Montefiore Hosp. and Medical Center, 111 East 210th St., Bronx, NY, 10467
JNCI; 69(1):15-22 1982

Striking differences in outcome of surgically treated colon adenocarcinomas were observed in 33 patients according to the DNA distribution patterns in tumor nuclei, measured by flow cytometry. As discussed and defined in the text and confirmed by appropriate control studies, the tumors were classified into two groups: predominantly diploid (20 tumors) and predominantly nondiploid (13 tumors). During the follow-up period of 3-5 yr. Twelve of the 13 patients with 'nondiploid' tumors died of disease within 4-34 mo, and the 1 patient still alive after 59 mo has extensive metastases. Only 6 of the 20 patients with 'diploid' tumors died of disease, sometimes after a slow, protracted clinical course. There were 14 patients with no evidence of disease for periods ranging from 30 to 60 mo; 1 of these patients died of other causes. Histologic grading and Dukes' staging appeared to play a relatively limited role in the outcome, although lymph node metastases and vascular invasion were more often observed in the nondiploid tumors. These observations suggest that the determination of DNA distribution in colon carcinomas may prove to be of prognostic value. (Author abstract) (40 Refs)

8. IMMUNOPEROXIDASE STAINING OF CARCINOEMBRYONIC ANTIGEN WITH MONOCLONAL ANTIBODIES IN ADENOCARCINOMA OF THE COLON.

Lindgren J, Wahlstrom T, Bang B, Hurme M, Makela O
(c/o Wahlstrom) Dept. Pathology, Univ. Helsinki, Haartmaninkatu 3, SF-00290 Helsinki 29, Finland
Histochemistry; 74(2):223-227 1982

Application of monoclonal antibodies to the immunoperoxidase staining of carcinoembryonic antigen (CEA) is described. A distinct positive staining of the neoplastic epithelial cells was seen in all sections stained with unadsorbed anti-CEA ascites fluids and the rabbit anti-CEA-antiserum. All controls including the ascites fluids adsorbed with purified CEA were negative. The nonspecific background staining of the ascites fluids was negligible in all dilutions used giving a better distinction than the rabbit antiserum. (9 Refs)

9. THE VALUE OF CARCINOEMBRYONIC ANTIGEN AND TENNESSEE ANTIGEN IN DIAGNOSIS OF RECTAL CARCINOMA.

Brockamp G, Braun J, Langer S
Abteilung Chirurgie der Medizinischen Fakultat, RWTH Aachen, Goethestr. 27/29, D-5100 Aachen, W. Germany
Aktuel Chir; 17(3):99-101 1982

Forty-five patients with histologically confirmed adenocarcinoma of the rectum were tested preoperatively for carcinoembryonic antigen (CEA) and Tennessee antigen (TAG) in their sera. Abnormally high CEA levels were found in sera of 22 of the patients and abnormally high TAG levels in sera of 39. The TAG levels were abnormal in 21/23 patients with normal CEA levels, while the CEA levels were abnormal in 2/6 patients with normal TAG levels. No relationship was found between tumor stage and level of CEA or TAG. (30 Refs) (In GER)

10. IMMUNOLOGICAL SIMILARITY OF CEA AND ALPHA1-ACID GLYCOPROTEIN (OROSOMUCOID).

Ochi Y, Fujiyama Y, Hosoda S, Miyazaki T, Yoshimura M, Hachiya T, Kajita Y
Second Dept. Internal Medicine, Shiga Univ. Medical Science, Seta, Otsu, Shiga, 520-21, Japan
Clin Chim Acta; 122(2):145-160 1982

Carcinoembryonic acid (CEA) labeled with 125I could be precipitated by antibody to alpha1-acid glycoprotein (AG) in a dose-dependent manner. CEA preparations showed cross reactivity with three kinds of commercial anti-AG preparations by polyethylene glycol and by a double antibody method. The radioactive peak of 125I-CEA showed cross-reactivity with commercial anti-AG and with antisera to purified AG preparations. The binding of 125I-CEA with anti-AG was displaceable by purified AG. Thus, CEA and AG are immunologically similar, although antibody against CEA showed no cross-reactivity with AG. The CEA molecule may have a component that is immunologically similar to AG and it may be in the protein part. CEA purified from hepatic metastases of a primary adenocarcinoma of the colon was subjected to anti-AG sepharose affinity chromatography, eluted and labeled with 125I. Fractionation revealed a peak with extremely high immuno-reactivity with both anti-AG and anti-CEA and a large molecular protein with both AG and CEA antigenic determinants. Studies of the immunoreactivity of this large mol wt fraction demonstrated that the immunoreaction of CEA with anti-AG was a non-precipitation reaction. Based on differences in binding affinities between CEA with anti-CEA and with anti-AG, it was postulated that CEA may be a biosynthetic precursor of AG or pro-AG. (38 Refs)

11. ANTIGENS OF THE BASEMENT MEMBRANE AND THE PERITUMORAL STROMA IN HUMAN COLONIC ADENOCARCINOMAS: AN IMMUNOFLUORESCENCE STUDY.

Burtin P, Chavanel G, Foidart JM, Martin E
Laboratoire d'Immunochimie, Institut de Recherches Scientifiques sur le Cancer, B. P. 8, 94802 Villejuif Cedex, France
Int J Cancer; 30(1):13-20 1982

Twenty colonic adenocarcinomas were studied by immunofluorescence with antisera against components of the basement membrane: Type IV collagen, laminin and heparan sulfate-rich proteoglycan, as well as antisera against antigens of the connective tissue: Type-III collagen, fibronectin and hyaluronectin. Marked alterations of the basement membranes were consistently observed on staining with each one of the first three antisera. In contrast, staining of the normal components of connective tissue was in most cases as intense as in normal colonic mucosa. Hyaluronectin, a marker of peritumoral stroma, was found to be present in 12 out of 15 tumors studied. (Author abstract) (22 Refs)

12. FIBRIN CLOT RETRACTILE (FCR) ACTIVITY OF FIBROBLAST-LIKE CELLS FROM NORMAL INDIVIDUALS AND CANCER PATIENTS.

Curatolo L, Borgia R, Donati MB, Morasca L
Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
Cell Biol Int Rep; 6(6):609-618 1982

Changes in fibrin clot retractile activity (FCRA) were studied under standardized conditions in fibroblasts from healthy donors of various ages, subjects with genetic abnormalities, and various types of cancer patients. Cells were serially cultured in Eagle's minimum essential medium on Hank's balanced salt soln plus 10% bovine serum. Cells usually were tested at least 10 passages before the end of the culture. The test system involved retraction of fibrin clots formed by clotting a mixture of test cells and platelet-free plasma with thrombin. A constant concentration of 1 x 10(6) cells/ml was used and results were reported 24 hr after incubation of the clot at 37 C. Cells with a finite replicative life still had high FCRA late in their lifespan. FCRA was completely lost in cells with an infinite replicative lifespan. FCRA was sometimes reduced in fibroblasts from the skin of patients with colorectal adenomatosis and a Kirsten sarcoma virus infected line. A group of human fibroblasts from cancer patients was unable to induce FCRA. No difference was found in FCRA of cells from normal embryos or adults. The role of fibrin in relation to the spread of cancer is discussed. (22 Refs)

13. FECAL NEUTRAL STEROLS IN PATIENTS WITH COLON CANCER.

Perogambros A, Papavassiliou J, Legakis NJ
Dept. Microbiology, Sch. Medicine, Univ. Athens, PO Box 1540, Athens, Greece
Oncology; 39(5):274-278 1982

Fecal cholesterol and its metabolites were measured in 10 patients with colon cancer and 10 control subjects. All individuals were consuming a mixed western diet at the time of collection of stool specimens. The fecal concentration of total neutral sterols and coprostanol was greater in the control subjects as compared to the colon cancer patients, but the difference was not statistically significant. The same was the case for the metabolic conversion rate of cholesterol. The frequency of the latter was bimodal especially among control subjects, with three subjects having an extremely high conversion rate. The level of neutral sterols is lower from stated values in most reports for colon cancer patients but higher to that reported for high risk populations for colon cancer and to this respect our findings are relevant with the increasing incidence of colon cancer in Greece. (Author abstract) (38 Refs)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

14. MANAGEMENT AND SURVIVAL OF ADENOCARCINOMA OF THE RECTUM IN THE UNITED STATES: RESULTS OF A NATIONAL SURVEY BY THE AMERICAN COLLEGE OF SURGEONS.

Mettlin C, Natarajan N, Mittelman A, Smart CR, Murphy GP
Roswell Park Memorial Inst., 600 Elm St., Buffalo, NY, 14263
Oncology; 39(5):265-273 1982

Data from the long- and short term surveys of the American College of Surgeons Commission on Cancer were examined to evaluate the survival and management of patients with rectal cancer in the United States. Overall, females experienced better survival than males, and whites had better survival than blacks. The 5-yr survival rates for localized, regional and distant stages of the disease were 76.4, 43.1, and 5.5%, respectively. The survival rates in relation to histologic grade of the tumor indicated that the survival experiences of patients with well and moderately differentiated tumors were similar (57% versus 54%) and that patients with poorly differentiated tumors had significantly lower survival (35%). The survival experience of those receiving abdominoperineal resection was similar to those treated by low anterior resection (56% versus 58%). Location of the tumor in the rectum did not affect prognosis. (Author abstract) (27 Refs)

15. CANCER OF THE RECTUM AND RECTOSIGMOID JUNCTION. RESULTS AND SELECTION CRITERIA FOR SURGICAL TREATMENT (ANALYSIS OF 563 CASES).

Aureggi A, DiGiorgio A, Angrisani A, Virno F, Bolognese A, Stipa V
Istituto di I Clinica Chirurgica, Universita degli Studi di Roma, Rome, Italy
Minerva Chir; 37(7):611-622 1982

Carcinoma of the rectum or rectosigmoid junction was diagnosed in 563 patients (59.3% men and 40.7% women) during the period 1950-1980. Radical surgery was performed in 433 patients, palliative surgery in 80 and exploratory laparotomy in 17 of the 530 patients subjected to surgery. Radical surgery included abdominoperineal amputation (APA) according to Miles' technique in 182 patients, colorectal resection with pull-through technique (CRR) in 152, anterior resection with skeletonizing of the inferior mesenteric artery (ARS) in 38, anterior resection with ligation of the inferior mesenteric artery (ARL) in 37, colorectal resection according to Hartmann's technique (CRH) in 20, transanal excision in 2 and posterior resection in 2. Extended surgery was performed in 63/433 patients. The postoperative complication rates were 20/182 after APA, 15/75 after anterior resection, 25/152 after CRR and 2/20 after CRH. The postoperative mortality rates were 16/182 after APA, 7/75 after anterior resections, 8/152 after CRR and 2/20 after CRH. The overall 5-yr survival rate, determined for 288 of the patients subjected to radical surgery, was 55.5%, showing no significant differences as a function of the type of surgery or tumor location, but being dependent on the tumor stage established intraoperatively. (29 Refs) (In ITA)

16. RESULTS OF EXTENDED SURGERY FOR CANCER OF THE RECTUM AND SIGMOID.

Bonfanti G, Bozzetti F, Doci R, Baticci F, Marolda R, Bignami P, Gennari L
Oncologia Clinica G, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy
Br J Surg; 69(6):305-307 1982

The clinical records of 61 patients who underwent extended surgery, including resection of parietes or other viscera, from 1965 to 1977 for cancer of the rectum and sigmoid were reviewed. Abdominoperineal resection was performed in 41 patients, anterior resection in 18 and Hartmann's resection in 2. The postoperative mortality rate was 8.2%, the non-lethal morbidity rate 30.3%, but four patients presented multiple complications. The 5-yr survival rate was evaluated separately for patients with and without microscopic evidence of neoplastic involvement of the simultaneously excised structures; in the first group it was 32%, in the second 75%. Local or distant recurrence occurred in 66% of patients with microscopic infiltration and in 24% of patients without microscopic infiltration. These results compare favorably with those reported after ordinary resections of Dukes' C cancers of the rectum and sigmoid, and seem to justify the use of extended surgery when cancer of the rectum and sigmoid has invaded contiguous structures. (Author abstract) (15 Refs)

17. RESECTION AND SUTURED COLO-ANAL ANASTOMOSIS FOR RECTAL CARCINOMA.

Parks AG, Percy JP
St Mark's Hosp., City Road, London ECIV 2PS, England
Br J Surg; 69(6):301-304 1982

Resection with preservation of the anal sphincters is now widely accepted as providing satisfactory treatment for carcinoma of the upper rectum. However, restorative resection is less widely performed for tumors of the lower rectum because anastomosis can be technically difficult when performed low in the pelvis. Between 1973 and 1980, 76 patients with rectal carcinoma underwent rectal resection and restoration of bowel continuity by means of a sutured anastomosis between colon and anal canal. The pathological characteristics of these tumors were similar to those of all cases of carcinoma of the rectum treated at St Mark's Hospital between 1948 and 1972. Two patients developed pelvic sepsis following colonic necrosis and anastomotic breakdown. Eight developed pelvic sepsis without major anastomotic breakdown. No patient died as a result of pelvic sepsis. Sixty-nine of the 70 patients who were able to be assessed were either completely normal functionally or had only minor deficiencies of bowel function. Six patients have been observed to develop recurrent pelvic tumor, localized to the pelvis in four patients and concurrent with the development of widespread metastases in two. Twenty-one of 32 patients are alive 3 yr and 12 of 19 patients are alive 5 yr after a curative operation for rectal carcinoma. These results are comparable with those seen following total excision of the rectum and pelvic floor for similarly sited tumors. (Author abstract) (25 Refs)

18. THE ROLE OF PRE-OPERATIVE ADJUVANT THERAPY IN THE MANAGEMENT OF BORDERLINE OPERABILITY RECTAL CANCER.

Wassif SB
Rotterdamsch Radio-Therapeutisch Instituut (RRTI), Groene Hilledijk 301, 3075 EA Rotterdam, The Netherlands
Clin Radiol; 33(3):353-358 1982

One hundred and forty-three patients with potentially operable primary rectal cancer (of stage T2, T3 and T4), were allocated to one of three regimens of therapy, ie surgery only (S), preoperative radiotherapy followed by surgery (R), or preoperative radiotherapy combined with daily intravenous fluorouracil during the first 4 days of irradiation followed by surgery (C). The adjuvant therapy was well tolerated. It had no adverse effects on surgical procedures or morbidity. There was improvement in the resectability rate C greater than R greater than S, and reduction in the incidence of Duke's C category in the surgical specimens C less than R less than S. Five-yr follow-up analysis showed marked differences in the local control rates, and a reduced incidence of liver metastases in Group C. There was no significant difference in survival overall between the three treatment groups, but when patients with T3 and T4 tumors were analyzed separately there was a statistically significant improved 5-yr survival in Group C (p less than 0.01) when compared to Group S, while Group R gave a marginally significant result when compared to Group S (p = 0.05). (Author abstract) (9 Refs)

19. SPHINCTER-SAVING SURGERY IN CANCER OF THE DISTAL REGION OF THE RECTUM.

Amelina OP, Ianovol VV, Levchenko NR
Dept. Surgery, Medical Inst., Blagoveshchensk, USSR
Vestn Khir; 128(5):39-43 1982

Of 500 patients with cancer of the distal third of the rectum, 32 (17 men, 15 women; 80% were greater than 50 yr) underwent sphincter-saving abdominal-perineal operations. One patient died during the early postoperative period. Postoperative complications included wound suppuration (7), and necrosis of the pulled-through intestine (1). Long-term results were followed-up in 27 patients. All were free of recurrences; 50% survived for 2-5 yr. (7 Refs) (In RUS)

20. A CLINICAL AND PHYSIOLOGICAL EVALUATION OF BOWEL PREPARATION FOR ELECTIVE COLORECTAL SURGERY.

Keighley MR, Condon RE
General Hosp., Steelhouse Lane, Birmingham B4 6NH, England
World J Surg; 6(4):464-470 1982

Methods of mechanical bowel preparation for elective colorectal surgery; patient accepatability; efficiency in removal of fecal residue; influence of preparations on electrolyte and fluid balance, fecal microflora, and on postoperative sepsis; and explosive potentialof gases in bowel preparation are discussed. The method of bowel cleansing combines administration of an oral hyperosmolar soln with intestinal lavage through a nasogastric tube. Mannitol, salina lavage, and antibiotics are recommended in most patients, except for patients with tumors associated with severe stenosis of the left colon. (34 Refs)

21. THE FLEXIBLE IMPLANT IN TREATMENT OF RECTAL CARCINOMAS.

Vider M, Lim N, Ditlow R, Au F, Gennaro AR
Dept. Radiation Oncology, Univ. Tennessee Center Health Sciences, Walter F. Chandler Building, 865 Jefferson Ave., Memphis, TN, 38163
J Surg Oncol; 20(3):157-160 1982

A modified technique for removable afterloading Iridium-192 implantation is described. Under local or general anesthesia, a series of flexible tygon tubes are introduced into all the tumor area in the rectum. This technique is especially suitable for palliation in high-risk, elderly patients. No rectal tube is necessary in this technique. (Author abstract) (11 Refs)

22. PHARMACOKINETICS OF MITOMYCIN C IN RABBIT AND HUMAN.

van Hazel GA, Kovach JS
(c/o Kovach) Div. Developmental Oncology, Mayo Clinic, 200 First Street Southwest, Rochester, MN
Cancer Chemother Pharmacol; 8(2):189-192 1982

Plasma elimination and urinary excretion patterns of mitomycin C were evaluated using a newly developed non-ionic high pressure liquid chromatographic technique. This technique allowed the complete separation of mitomycin C from porfiromycin. Two patients, one with advanced lung cancer and one with advanced colon cancer, received mitomycin C alone at 15 mg/square meter (m2). One further patient with advanced lung cancer received mitomycin C, 8 mg/m2. There was a rapid distribution and relatively rapid elimination of mitomycin C from plasma in all three patients. The longest secondary half-life of plasma elimination was in the lung cancer patient, who had abnormal liver function. The secondary half-life of elimination of mitomycin C from the plasma of treated rabbits (range 7.1-12.1 min) was significantly less than that observed in the three patients (35-62 min). This was thought to be due to differences in the rate of metabolism of the drug. (17 Refs)

23. PHASE II EVALUATION AND PLASMA PHARMACOKINETICS OF HIGH-DOSE INTRAVENOUS 6-THIOGUANINE IN PATIENTS WITH COLORECTAL CARCINOMA.

Konits PH, Egorin M, Van Echo DA, Aisner J, Andrews PA, May ME, Bachur NR, Wiernik PH
(c/o Egorin) Medical Oncology Section, Baltimore Cance Res. Center, Univ. Maryland Hosp., 22 South Greene St., Baltimore, MD, 21201
Cancer Chemother Pharmacol; 8(2):199-203 1982

Nineteen patients (13 males, 6 females) with histologically proven metastatic adenocarcinoma of the colon or rectum were treated with 57 iv courses of 6-thioguanine (6TG). 6TG was administered as a 30 min infusion every 3 wk. The initial iv dose was 700 mg/square meter (m2), although two patients with liver metastases and bilirubins greater than 30.0 were started at 350 mg/m2. Later in the trials, one patient received a starting dose of 900 mg/m2, four patients received a starting dose of 1,200 mg/m2. No patient had a therapeutic response from 6TG, although ten patients with previously progressive disease achieved stabilization lasting from 10-32 wk. The major toxic side-effect was leukopenia. 6TG and several of its metabolites were detected in the plasma of patients. Concentrations of 6TG rose during infusion, peaking at 61-118 nmol/ml. Following infusion 6TG concentrations declined in bi-exponential fashion. Several known metabolites of 6TG were also observed in plasma. It was concluded that iv intermittent high-dose 6TG has little activity against colorectal cancer and that further trials do not seem warranted. (10 Refs)

24. COMBINED METHYL-CCNU, VINCRISTINE, 5-FLUOROURACIL, AND STREPTOZOTOCIN IN THE TREATMENT OF ADENOCARCINOMA OF ADVANCED COLORECTAL CANCER. A PILOT STUDY.

Tognl P, Sessa C, Varini M, Cavalli F
(c/o Cavalli) Servizio oncologico, Ospedale San Giovanni, CH-6500 Bellinzona, France
Schweiz Med Wochenschr; 112(26):930-933 1982

Sixteen patients with advanced colo-rectal cancer were treated with the combination methyl-CCNU (semustine), vincristine, 5-fluorouracil and streptozotocin (MOF-Strepto). Seven cases were previously untreated. A partial remission was observed only in one patient (6%, confidence limits to 95%: 1-17%). Marked gastrointestinal and hematologic toxicity was registered. Based on this experience the authors are unable to confirm other pilot studies claiming major antitumor activity for MOF-Strepto in the treatment of advanced colo-rectal cancer. (Author abstract) (27 Refs) (In FRE)

25. ADJUVANT PORTAL HEPATIC PERFUSION IN PATIENTS WITH COLORECTAL CARCINOMA: A SWISS MULTICENTER STUDY.

Metzger U, Aeberhard P, Egeli RA, Harder F, Largiader F, Muller W, Pettavel J, Weber W, Cavalli F
Chirurgische Klinik A, Universitatsspital, CH-8091 Zurich, Switzerland
Helv Chir Acta; 49(1/2):175-178 1982

The effectiveness of adjuvant portal hepatic perfusion (APHP) in preventing hepatic metastases was studied in approx 40 patients who had undergone complete resection of colorectal carcinomas. A venous catheter was placed in the portal vein via the umbilical vein or a mesenteric branch; the procedure was guided radiologically. Patients received 500 mg 5-fluorouracil (FU)/square meter (m2) of body surface area and 10 mg mitomycin C (MMC)/m2 by continuous perfusion. FU was given immediately after surgery and continuing over 7 days. MMC was given as a single dose on the day after surgery. The catheter was removed after 7 days. Twenty patients completed treatment according to plan. No complications occurred in association with implantation or removal of the catheter. APHP did not alter liver function or laboratory parameters or produce myelosuppression in any of the 20 patients. Wound healing was not affected by APHP. Early postoperative changes were more likely to result from surgery or general anesthesia than from APHP. Findings indicate the practical use of APHP in a multicenter study. A prospective, randomized, controlled study of APHP is now in progress. (5 Refs) (In GER)

OTHER CLINICAL AND PRECLINICAL ASPECTS OF COLORECTAL NEOPLASMS

26. NATURAL HISTORY OF HEREDITARY CANCER OF THE BREAST AND COLON.

Albano WA, Recabaren JA, Lynch HT, Campbell AS, Mailliard JA, Organ CH, Lynch JF, Kimberling WJ
Inst. Familial Cancer Management and Control Incorporated, 2500 California, Omaha, NE, 68178
Cancer; 50(2):360-363 1982

The natural history of 106 patients from 18 families manifesting hereditary breast cancer syndromes, and 117 affected patients from 20 families manifesting nonpolyposis hereditary colon cancer were evaluated. Findings were compared with the American College of Surgeons (ACS) long-term audits for breast and colon cancer respectively. The cardinal features of hereditary cancer were observed within the study group, including: (1) a significant younger age of onset (49 years, breast; 46 yr, colon); (2) an excess of proximal lesions in the hereditary colon series (49%); and (3) an excess of bilaterality in the hereditary cancer patients. The clinical stage at presentation was similar for the hereditary and ACS audit patients. Five-yr survival was significantly improved (p less than 0.05) for both hereditary cancer populations are compared to the ACS audits (67% hereditary breast cancer and 52% nonpolyposis hereditary colon cancer). Improved survival in hereditary colon and breast cancer patients may have a bearing on the design of future clinical protocols. (Author abstract) (15 Refs)

27. INVOLVEMENT OF UPPER REGION OF THE DIGESTIVE TRACT IN PATIENTS WITH COLONIC CANCER.

Kolesnikova GD, Kapuller LL, Vorob'ev GI
Res. Inst. Proctology, Moscow, USSR
Khirurgiia (Mosk); (5):59-62 1982

Of 609 patients with colorectal cancer, 16 (44-71 yr old) had primary multiple tumors of the gastrointestinal tract. Ten patients had synchronous tumors (8 had solitary tumors and 2 had multiple exophytic tumors of the large intestine). Of 10 patients, 7 had large adenocarcinomas of the stomach and 3 had advanced colonic and stomach tumors with peritoneal and liver metastases. Primary multiple metachronous tumors were diagnosed in six patients. One patient developed cancer of the rectum 12 yr after surgery for stomach cancer, while five patients developed stomach cancer within 1-7 yr after surgery for colonic cancer. Of six patients, five had solitary gastrointestinal tumors and one had multiple stomach adenocarcinomas. These findings indicate that the patients subjected to surgery for colonic neoplasms should undergo repeated endoscopic examination. (10 Refs) (In RUS)

28. CARCINOMA OF RECTUM (RESULTS OF TWENTY YEARS FOLLOW UP).

Singh RP, Salazar C, Littlefield JB
Marshall Univ. Sch. Medicine, Huntington, WV
Am J Proctol Gastroenterol Colon Rectal; 33(6):14-15,24 1982

This is a retrospective study reviewing the survival of 122 cases of cancer of the rectum, followed for 20 yr. From the study it is apparent that 5-and 10-yr survival is not good enough. The patients continue to die from metastatic disease on long-term follow up. Younger patients and Whites showed better survival at 20 yr; 40% of Duke A, 25.7% of Duke B, 27.7% of Duke C and none of the Duke D patients survived 20 yr. Patients (39.4%) treated by abdominoperineal resection survived 20 yr. Though this series is too small; however, it makes a reasonable point of following the patients with cancer of the rectum for 20 yr or more. This would enable us to arrive at a more accurate conclusion on the long-term survival of these patients. (Author abstract) (11 Refs)

29. THROMBOEMBOLIC DISEASE IN PATIENTS WITH MALIGNANCY (A CLINICAL STUDY OF 198 TUMOR PATIENTS).

Honegger HP, Tullis JL
Abteilung fur Onkologie, Departement fur Innere Medizin, Universitatsspital, CH-8091 Zurich, Switzerland
Praxis; 71(22):955-959 1982

The incidence of thromboembolic disease (TE) was studied in 198 patients (80 men, 23-83 yr old, av 60.0 yr old; 118 women, 25-88 yr old, av 59.2 yr) with various malignant tumors. Tumors included 43 lung, 41 breast, 25 colorectal, 14 upper gastrointestinal, 15 female genital, 16 lymphoma, 10 prostatic, 6 pancreatic, 6 urinary, 6 sarcoma, and 16 miscellaneous tumors. Metastases were present in 136 patients. In the course of 5-20 mo (av 1 yr) all occurrences of TE, including thrombophlebitis, phlebothrombosis, pulmonary embolism, marantic endocarditis, and arterial embolism, were recorded. TE occurred 42x in 32/198 patients. Ten men (av 63 yr) and 22 women (av 58 yr) were affected by TE. Venous symptoms occurred in 28 cases. Eight patients showed spontaneous occurrence of phlebitis in two mutually independent sites without compression. Arterial ischemia occurred in four patients. Serial sections of tumor tissue showed embolisms in two patients. Marantic endocarditis was confirmed at autopsy in two patients. Pulmonary embolisms were found in six patients. Only one patient died of causes directly related to TE. No correlation was found between the occurrence of TE and particular tumor locations or histological types. TE occurred more frequently among patients with localized tumor growth than among those in remission or with metastatic tumors. Of coagulation parameters measured, only shortened partial thromboplastin time correlated with later occurrence of TE. (23 Refs) (In GER)

30. COLONOSCOPY AND COLON CANCER: CURRENT CLINICAL PRACTICE.

Overholt BF
Univ. Tennessee, Knoxville, TN
CA; 32(3):180-186 1982

Identification and elimination of carcinogenic factors predisposing to colon cancer, and a better understanding of intrinsic factors associated with this disease, are the ultimate goals of research in colorectal cancer. Until these goals are reached, early detection and elimination of precursor colorectal cancer lesions hold the greatest promise for reducing the incidence of this devastating cancer. Colonoscopy not only improves diagnostic capabilities but offers a relative safe and economic modality to eliminate the precursor lesion. As a result of colonoscopy and colonoscopic polypectomy, we can reasonably hope for and expect improved survival for colorectal cancer patients. The 1970s was a decade of technological development in colonoscopy. The decade of the 1980s promises major improvements in the survival rate of patients with colorectal cancer through colonoscopy and colonoscopic polypectomy. (Author abstract) (8 Refs)

31. A VILLOUS TUMOR OF THE APPENDIX. A CASE REPORT AND REVIEW OF THE LITERATURE.

Barre C, Chevalier J, Simon C, Goethals G, Pillet J, Enon B
Service de Chirurgie Generale, Centre Hospitalier Universitaire d'Angers, rue Haute de Reculee, 49000 Angers, France
Ann Chir; 36(5):349-352 1982

An unusual case of villous adenoma of the appendix (TAA), in a 69-yr-old man is presented. The patient presented with pain in the lower right quadrant. The patient underwent surgery for acute appendicitis. A large abscess of the appendix was discovered at surgery. Villous proliferation of the mucosa was one of the most significant postoperative histological findings. Appendectomy with regular colonoscopic follow-up examinations are recommended for cases of TAA. (27 Refs) (In FRE)

32. HUMAN COLORECTAL CARCINOMA: PATTERNS OF SENSITIVITY TO CHEMOTHERAPEUTIC AGENTS IN THE HUMAN TUMOR STEM CELL ASSAY.

Agrez MV, Kovach JS, Beart RW, Rubin J, Moertel CG, Lieber MM (c/o Lieber), Mayo Clinic, Guggenheim Building, Rochester, MN, 55905
J Surg Oncol; 20(3):187-191 1982

The human tumor stem cell assay (HTSCA) was applied to 103 primary and metastatic colorectal carcinomas. Thirty-four carcinomas could not be evaluated for colony formation (clonogenicity) because of microbial contamination. Of the remaining 69 carcinomas, 18 (26%) demonstrated clonal growth in vitro. Colony formation did not correlate with the clinicopathologic stage of the tumor, the histological grade of the tumor, the method used to disperse the solid tumors into single cells (mechanical or enzymatic), or cell viability (exclusion of trypan-blue) prior to plating. The in vitro chemotherapy sensitivity data of the 18 tumors which formed colonies indicated that most tumors were generally resistant to chemotherapeutic drugs and that a few tumors were sensitive to multiple agents. Use of the human tumor stem cell assay may facilitate an individualized approach to clinical chemotherapy of colorectal carcinoma for certain patients. (Author abstract) (13 Refs)

33. KARYOTYPE CONSISTENCY IN HUMAN COLORECTAL CARCINOMA CELL LINES ESTABLISHED IN VITRO.

Chen TR, Hay RJ, Macy ML
American Tissue Culture Collection, 12301 Parklawn Dr., Rockville, MD, 20852
Cancer Genet Cytogenet; 6(2):93-117 1982

Karyotypes of nine human colorectal cell lines deposited with the ATCC were studied by trypsin-Giemsa banding. CCL 229,230,231 and 235 belong in the stable type that is characterized by karyotypes consisting mostly of normal chromosomes and stable markers. CCL 228, 234, and 238 being in the unstable type that has karyotypes consisting of numerous markers in addition to normal chromosomes and stable markers. The remaining intermediate type has karyotypic characteristics between the above two types usually with two or less unstable markers per cell. The stable markers (together with normal chromosomes) are constitutive components of a cell genome and are common to most cells within the same cultured population. Unstable markers are the likely cause of karyotypic variations between cells and often are produced by balanced inter- and intrachromosome changes, or both. Consequently, total chromosome length per cell genome is remarkably consistent within a cell population, and karyotypes between cells are profoundly stable and mostly identical. Chromosome deletions and interhomologue exchanges had the highest incidences among both stable and unstable markers. The complex markers occurred relatively infrequently. There were neither common markers nor unique chromosome breakages common to all of these established cell lines. The significance of chromosome changes involving No 7 in this as well as other tumor pathotypes is briefly discussed. (35 Refs)

34. CHANGES IN [3H]GALACTOSE UPTAKE IN HUMAN COLONIC MUCOSA WITH CARCINOMA: AN ULTRASTRUCTURAL STUDY.

Dawson PA, Filipe MI
Dept. Histopathology, Westminster Medical Sch., Udall St., London SW1P 2PP, England
Histochem J; 14(3):361-383 1982

Uptake of [3H]galactose was studied by electron microscopical autoradiography both on the basis of isotope uptake over a period of time and with pulse labeling to investigate the changes in the glycoprotein synthesis associated with malignancy in the colonic mucosa. Normal mucosa and mucosa adjacent to tumor ('transitional') from human large bowel specimens resected for carcinoma were compared. The most marked differences were found in the middle and upper crypt; the region of differentiation being the middle crypt in all types of tissue and the upper crypt being a region of extended immaturity in transitional mucosa. (24 Refs)

35. UPTAKE OF [3H]THREONINE IN HUMAN COLONIC MUCOSA ASSOCIATED WITH CARCINOMA: AN AUTORADIOGRAPHIC ANALYSIS AT THE ULTRASTRUCTURAL LEVEL.

Dawson PA, Filipe MI
Dept. Histopathology, Westminster Medical Sch., Udall St., London SW1P 2PP, England
Histochem J; 14(3):385-401 1982

[3H]Threonine uptake was studied by electron microscopical autoradiography using the method of statistical analysis of Blackett and Parry. The results are discussed in the light of [3H]galactose studies. The changes in protein uptake are compared with different isotope incubation periods and with pulse-labeling techniques. Mean reactive values, including the standard errors, for the control and the 'transitional' mucosa with [3H]threonine labeling for the various organelles are presented. Results indicated that the increased uptake of [3H]threonine in transitional mucosa appears to be the result of prolonged protein synthesis associated with an extension of the cellular proliferation zone in the crypt rather than being an effect of increased cell turnover. (14 Refs)

36. CHARACTERISTICS OF SEVEN CLONES OF THE WIDR HUMAN COLON ADENOCARCINOMA CELL LINE.

Petricciani JC, Smith P, Earley EM, Levenbook I, Noguchi P
Bureau Biologics, Food and Drug Admin., 8800 Rockville Pike, Bethesda, MD, 20205
In Vitro; 18(5):492-494 1982

Seven clonal populations were derived from the WiDr human colon adenocarcinoma cell line and were characterized with respect to chromosome number. DNA content, and tumorigenicity in nude mice. There was no correlation between tumor vol and either DNA content or chromosome number; but there were wide differences among the clones regarding the size of tumors they were able to produce in nude mice. (author abstract) (8 Refs)

37. THE EFFECT OF DERIVATIVES OF FOLIC ACID ON THE FLUORODEOXYURIDYLATE-THYMIDYLATE SYNTHETASE COVALENT COMPLEX IN HUMAN COLON XENOGRAFTS.

Houghton JA, Schmidt C, Houghton PJ
Dept. Biochemical and Clinical Pharmacology, St. Jude Children's Res. Hosp., 332 North Lauderdale, Memphis, TN, 38101
Eur J Cancer Clin Oncol; 18(4):347-354 1982

This study was designed to examine the endogenous concentrations of 5,10-methylenetetrahydrofolate (CH2FH4) in human colorectal adenocarcinoma xenografts, and to determine the ability of other folate derivatives to increase the formation of the ternary covalent complex between CH2FH4, [6-3H]-5-fluorodeoxyuridylate (FdUMP) and thymidylate synthetase (TS, EC 2.1.1.45). Levels of CH2FH4 were determined by measuring the release of [3H]2O from [5-3H]-dUMP using TS from Lactobacillus casei. The reaction was linear from 1.9 x 10(-13) to 2.4 x 10(-11) mol of CH2FH4 assayed. Concentrations of CH2FH4 were low, ranging from 66 to 233 nM in cell water. Tetrahydrofolate (FH4) and dihydrofolate (FH2) and 5-methyltetrahydrofolate (5-CH3FH4) decreased the covalent binding of [6-3H]-FdUMP in vitro. Administration of FH4 or FH2 to tumor-bearing mice reduced subsequent formation of the covalent complex in vitro. Since 5-CH3FH4 is a major derivative of folate in mammalian tissues, its effect on the covalent binding of [6-3H]-FdUMP was examined further; even in the presence of homocysteine and cyanocobalamin (B12), the formation of the covalent complex was not increased. The fate of [5-14CH3]-FH4 was subsequently examined in vivo. In tumors at 1 hr after injection, 72% of the radiolabel remained as [5-14CH3]-FH4, while 17% had been converted to [14C]-methionine or incorporated into protein. By contrast, however, the incorporation of radiolabel into the protein fraction of liver was almost 30-fold greater at this time. At 4 hr, radioactivity in tumors (dpm/g) and in the fraction associated with [5-14CH3]-FH4 was decreased by over 60%, while metabolism was increased by only 13%. No polyglutamate forms of [5-14CH3]-FH4 were detected in tumors at 4 hr after treatment. (Author abstract) (38 Refs)

38. GROWTH CHARACTERISTICS OF HUMAN COLONIC ADENOCARCINOMAS PROPAGATED IN THE ROWETT ATHYMIC RAT.

Stragand JJ, Drewinko B, Henderson SD, Grossie B, Stephens LC, Barlogie B, Trujillo JM
(c/o Drewinko) Section Hematology, Dept. Lab. Medicine, Univ. Texas, M.D. Anderson Hosp. and Tumor Inst., Texas Medical Center, 6723 Bertner Ave., Houston, TX, 77030
Cancer Res; 42(8):3111-3115 1982

Two human colonic adenocarcinoma cell lines were propagated in the Rowett athymic rat. Line LoVo displayed a well-differentiated morphology and exhibited progressive growth over a 70-day observation period with a doubling time of 8.5 days throughout. No metastatic involvement was noted. Xenografts of SW 620 cells were undifferentiated and highly necrotic. These tumors grew progressively for approximately 30 days with a doubling time of 5.5 days, but over 90% of the animals exhibited a spontaneous regression with a mean time to total regression of 51 +-3 (SE) days. Animals which had rejected the SW 620 xenografts would not support the growth of either the SW 620 or LoVo xenografts when challenged a second time with inocula producing a 100% tumor incidence in control rats. No metastatic involvement was noted for the SW 620 xenografts, but the tumors frequently invaded the underlying musculature and protruded into the peritoneal cavity without producing ascites or tumor nodules at sites distant from the primary. (Author abstract) (24 Refs)

39. PHOSPHORIBOSYL PYROPHOSPHATE, POOL SIZE AND TISSUE LEVELS AS A DETERMINANT OF 5-FLUOROURACIL RESPONSE IN MURINE COLONIC ADENOCARCINOMAS.

Ardalan B, Villacorte D, Heck D, Corbett T
Div. Medical Oncolology, Univ. Southern California Comprehensive Cancer Center, GH 10-440, 2025 Zonal Ave., Los Angeles, CA, 90033
Biochem Pharmacol; 31(11):1989-1992 1982

The antitumor activity of 5-fluorouracil (FUra) in four murine colonic adenocarcinomas was correlated with the basal pool sizes of phosphoribosyl pyrophosphate (PRPP). Mice inoculated with murine colonic adenocarcinomas 26 and 38 (FUra-sensitive), and 51 and 11A (FUra-resistant), were treated approx 2 weeks later with FUra. Four hr following ip injection of FUra at 200 mg/kg, the group of enzymes which could perturb PRPP pool size were assayed, namely phosphoribosyl pyrophosphate synthetase (EC 2.7.6.1), hypoxanthine-guanine phosphoribosyl transferase (EC 2.4.2.8), adenine phosphoribosyl transferase (EC 2.4.2.7), and orotate phosphoribosyl transferase (EC 2.4.2.10). The specific activity of PRPP synthetase in the FUra-sensitive line was three-fold higher than in the FUra-resistant tumors examined; moreover, only in the sensitive line was the specific activity of orotate phosphoribosyl transferase increased significantly following treatment with FUra. Thus, these data suggest that measurement of the basal intratumoral PRPP levels, together with the determination of specific activities of PRPP synthetase and orotate phosphoribosyl transferase, should be tested for its potential clinical application as a means of selecting patients with gastrointestinal and breast carcinomas to be treated with FUra. (27 Refs)

40. INHIBITION OF DEVELOPMENT OF METHYLNITROSOUREA-INDUCED RAT COLONIC TUMORS BY PERORAL ADMINISTRATION OF INDOMETHACIN.

Narisawa T, Sato M, Sano M, Takahashi T
Dept. Surgery, Akita Univ. Sch. Medicine, Hondo 1-1-1, Akita 010, Japan
Gan; 73(3):377-381 1982

The nonsteroid anti-inflammatory drug indomethacin, a prostaglandin synthesis inhibitor, inhibited the development of carcinogen-induced large bowel carcinomas in rats. CD-Fischer rats were given carcinogenic pretreatment with intrarectal instillation of 2 mg of methylnitrosourea 3x a wk from the 1st to the 5th wk, in order to produce large bowel tumors. Thereafter, peroral administration of a high or low dose of indomethacin dissolved in drinking water (20 ug or 10 ug indomethacin/ml tap water) for 15 wk was started at the 11th wk, before the tumors developed. At autopsy in the 26th wk just after the completion of the 15-wk treatment, the incidence of developing large bowel tumors was significantly reduced in treated rats, compared to untreated control rats; 17% or 14% vs 67%. However, at autopsy in the 36th wk, 10 wk after cessation of the treatment, the development of tumors in treated rats was significantly increased. Thus, indomethacin inhibited the development of methylnitrosourea-induced large bowel tumors in rats. The effectiveness of peroral administration of indomethacin was comparable to that of intraperitoneal administration. It is postulated that treatment with this drug may effectively prevent the development of large bowel cancer in patients at high risk. (Author abstract) (23 Refs)

41. SELENIUM AND THE ACUTE EFFECTS OF THE CARCINOGENS, 2-ACETYLAMINOFLUORENE AND METHYLAZOXYMETHANOL ACETATE.

Banner WP, Tan QH, Zedeck MS
(c/o Zedeck) Lab. Pharmacology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Res; 42(8):2985-2989 1982

Selenium inhibits the development of 2-acetylaminofluorene-induced hepatic tumors and methylazoxymethanol-induced colon tumors. It has been suggested that selenium exerts these protective effects by inhibiting metabolic activation of the carcinogen. We have studied the effects of selenium upon the acute inhibition of RNA and DNA synthesis induced by 2-acetylaminofluorene or methylazoxymethanol in intact liver, regenerating liver, and colon of weanling male Sprague-Dawley rats. Some animals received selenium in the drinking water (4 ppm) for 1 wk, while others received a single injection of selenium (1 mg/kg ip) prior to being treated with the carcinogens. No protection against the effects of the carcinogens on RNA or DNA synthesis was noted with either treatment of selenium. Disulfiram did protect against the 2-acetylaminofluorene-induced inhibition of hepatic RNA synthesis, and pyrazole prevented the inhibition of RNA synthesis induced by methylazoxymethanol in both liver and colon. Serum selenium levels are reported. The data indicate that selenium does not influence the acute alterations induced by the carcinogens 2-acetylaminofluorene or methylazoxymethanol and suggest that the tumor-preventive effects of selenium are probably due to a mechanism other than interference with carcinogen activation and interaction with cellular macromolecules. (Author abstract) (34 Refs)

42. ADENOSINE 3,5'-CYCLIC MONOPHOSPHATE DEPENDENT AND INDEPENDENT PROTEIN KINASE ACTIVITIES IN 1,2-DIMETHYLHYDRAZINE INDUCED RAT COLON CANCER.

Singh D, Loven DP, Stevens RH
Dept. Anatomy, Radiation Res. Lab., University Iowa, Iowa City, IA, 52242
Chem Biol Interact; 40(2):169-175 1982

The adenosine 3',5'-cyclic monophosphate (cAMP)-dependent and cAMP-independent kinase activities were measured in the 1,2-dimethylhydrazine (DMH) induced rat colon cancer and in untreated colon. Previous studies had shown that intestinal tumors induced by chronic exposure to DMH contained two-fold less intracellular cAMP. The present findings indicate that reduction in cAMP-dependent protein kinase activities also occur in colon cancer cells. Similar hydrogen ion dependence (pH 6-7) and approximate association constants (Ka approx 0.1 uM) were observed for the enzymes existing in both normal and tumor tissues, while the cAMP-dependent tumor protein kinase was found to phosphorylate phosvitin and casein to a greater degree. These recent findings are consistent with the concept that the concentrations of cAMP and activities of its associated enzyme system are inversely related to the cell proliferation state. (Author abstract) (22 Refs)

43. HYPERPLASIA AND HYPERPLASTIC POLYPS IN THE LARGE INTESTINE OF MICE DURING 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOGENESIS.

Krutovskikh VA
All-Union Cancer Res. Center, Moscow, USSR
Eksp Onkol; 4(3):20-25 1982

Development and potential malignant transformation of hyperplastic polyps of the large intestine were studied in male (CBA x C57BL)F1 mice exposed to 1,2-dimethylhydrazine (DMH: 16 mg/kg/wk, sc). Within different time periods after the initiation of DMH administration, the mice were sacrificed, and specimens of large intestine were subjected to scanning electron microscope examination. The DMH administration resulted in progressive changes in the ultrastructure of crypts. Hyperplastic exophytic nodules were first detected 10-15 wk after the initiation of the experiment. The number of nodules correlated with the degree of hyperplasia of the intestinal mucosa. Approx 5-10% of the hyperplastic polyps showed malignant transformation; spherical or saucer-like tumors with foci of tissue atypia were first detected after 20-wk administration of the DMH. All tumors observed after 25-30-wk administration infiltrated the intestinal wall. (14 Refs) (In RUS)

44. EFFECT OF A MARGINALLY LIPOTROPE-DEFICIENT DIET ON METHYLAZOXYMETHANOL ACETATE CARCINOGENESIS.

Kato K, Mori H, Takahashi M, Hirono I
Dept. Pathology, Gifu Univ. Sch. Medicine, Gifu, Japan
Nutr Cancer; 3(4):234-239 1982

The effect of a lipotrope-deficient diet on methylazoxymethanol acetate (MAM acetate) intestinal carcinogenesis was studied in 2 groups of ACI rats. For 10 wk, weanling rats were fed a semisynthetic diet that was either high in fat and marginally deficient in the lipotropes (Group 1), or adequate for rats in all known respects (Group 2). Four wk after the start of the experimental diets, the animals were given a weekly SC injection of MAM acetate, 25 mg/kg body weight, for a total of 5 times. Following the termination of the experimental diets, the animals were fed a basal diet until the end of the experiment (480 days). The tumor incidence in the jejunum-ileum and the number of tumors in the colon were significantly higher in Group 1 than in Group 2. These results suggest that a marginally lipotrope-deficient diet enhances MAM acetate carcinogenesis, probably in its early stage. (Author abstract) (14 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

45. SUMMARY OF A WORKSHOP ON CHOLESTEROL AND NONCARDIOVASCULAR DISEASE MORTALITY.

Feinleib M

Div. Heart and Vascular Diseases, Natl. Heart, Lung, and Blood Inst., Bethesda, MD, 20205

Prev Med; 11(3):360-367 1982

Data from 17 population studies concerning the question of whether very low cholesterol levels (usually below 180 mg/deciliter), while favorably affecting mortality rates from coronary heart disease, might be related to excess incidence and deaths from other causes including cancer were reviewed. Inconsistent relationships between cholesterol concentration and mortality from noncardiovascular disease and malignant neoplasms were found. Eight studies found an inverse relationship between serum cholesterol and mortality from malignant neoplasms in men; none found a significant association between these variables in women. Four studies found a significant inverse association between blood cholesterol and colon cancer in men; similar but not significant associations were seen in two other studies. No other specific sites of cancer exhibited a significant association in more than one or two studies. While the data did not substantiate any direct cause-and-effect relationship between low blood cholesterol and cancer, low blood cholesterol could possibly be a genetic 'marker' for a small number of cancer-prone males in a given population. No pathogenetic mechanism could be supported with the data reviewed. The current public health message recommending limitation of cholesterol intake by those with elevated cholesterol levels should not be changed based on the data reviewed, and physicians should continue to advise reduction of blood cholesterol levels for all persons exhibiting higher than normal levels. (13 Refs)

46. A CASE-CONTROL STUDY OF CHOLECYSTECTOMY AND RIGHT-SIDE COLON CANCER. THE INFLUENCE OF ALTERNATIVE DATA SOURCES AND DIFFERENTIAL INTERVIEW PARTICIPATION PROPORTIONS ON ODDS RATIO ESTIMATES.

Vernick LJ, Kuller LH
Illinois Cancer Council, 36 S. Wabash Ave., Suite 700, Chicago, IL, 60603
Am J Epidemiol; 116(1):86-101 1982

One hundred fifty patients with right-side colon cancer (ie, patients with adenocarcinoma of the cecum or ascending colon) were compared to 150 matched left-side colon cancer controls (ie, patients with adenocarcinoma of the descending or sigmoid colon) and to 123 neighborhood controls, Pittsburgh, Pennsylvania, Standard Metropolitan Statistical Area, 1975-1978. The gastrointestinal surgical history was ascertained for all study subjects so that the presence or absence of a history of cholecystectomy could be noted. Cholecystectomy history was obtained through telephone interviews and whenever possible subsequently validated from operative and pathology reports at time of cholecystectomy. Cholecystectomy history for the colon cancer patients was also abstracted from hospital records at time of colon cancer diagnosis with an attempt to confirm the gallbladder's status through operative reports, cholecystograms, and physical examinations. Hospital records and interviews for the colon cancer patients appeared to provide accurate exposure history. Point estimates of the odds ratios and confidence intervals for intra- and inter-data source comparisons (ie, hospital records, interviews, and hospital records and interviews combined) were comparable with similar measures of effect. Consistent odds ratio estimates appeared in both left-side colon cancer controls (1.9) and neighborhood controls (1.89). The authors suggest that changes in bile acid metabolism following cholecystectomy may be associated with an increased risk of right-side colon cancer. (Author abstract) (20 Refs)

47. THE PHYSIOLOGICAL IMPORTANCE OF THE COLONIC MICROFLORA.

Gustafsson BE
Dept. Germfree Res., Karolinska Inst., Box 60 400, S-104 01 Stockholm, Sweden
Scand J Gastroenterol [Suppl]; 17(77):117-131 1982

The present concept of the intestinal microflora has been reviewed with stressing the fact that it represents an entity with a wt comparable to one of the large organs of the body. It is composed of about 500 different strains, many of which as yet have not been isolated because 95% of them are anaerobic and fastidious in their growth requirements. The intimate relationship of the flora to the surface epithelium of the intestines and the Lieberkuhn's crypts are brought forward. The production of germfree animals is reviewed as an accounting of the most obvious differences between the germfree animal and its conventional counterparts, as far as gastroenterology is concerned. This includes the protective function of the normal intestinal flora, the cecum enlargement in germfree rodents, the influence of the flora on the metabolism of bilirubin, intestinal mucin, and pancreatic enzymes. Differences found in germfree animals due to the absence of the microbial flora related to the metabolism of fatty acids, bile acids, cholesterol and steroid hormones are also reviewed. The germfree animal has even proven to be an important research tool in such fields as carcinogenesis and studies of Crohn's disease and ulcerative colitis. There is need of a wider use of the germfree animal as a baseline in studies on the interference of the intestinal microbial flora with factors and conditions of great physiological and clinical importance. (Author abstract) (101 Refs)

48. MUTAGENS IN HUMAN FAECES. ARE THEY RELEVANT TO CANCER OF THE LARGE BOWEL?

Venitt S
Chester Beatty Res. Inst., Nightingales Lane, Chalfont St. Giles, Bucks HP8 4SP, England
Mutat Res; 98(3):265-286 1982

Bacterial mutation studies and cytogenetic studies of extracts of human feces (HF) and the role of mutagens in HF are reviewed. The hypothesis that colorectal cancer might be caused by carcinogenic chemicals generated endogenously by metabolism of fecal substrates by the gut microflora has been tested directly, using short-term assays which have been developed for detecting potential carcinogens. Studies on nitrate, nitrite, and nitrosamines in the intestinal tract (IT) showed that conditions in the lower IT favor denitrification rather than nitrification. Bacterial mutagens have been detected in fecal extracts obtained from several groups of subjects drawn from widely differing communities and consuming very different diets. Chromosome-damaging activity has also been demonstrated in extracts of HF, this latter finding being based on a very small sample group. Therefore, studies indicate that normal people regularly excrete feces which contains constituents possessing properties (mutagenicity and clastogenicity) characteristic of carcinogens. The possibility that the mutagenic activity of fecal extracts is artefactual cannot be excluded until extraction and mutagenesis assays are preformed under anaerobic conditions. Apart from the metabolic activity of fecal flora occupying the colonic lumen, the colonic epithelium itself possesses enzyme systems capable of metabolizing xenobiotics to mutagenic derivatives. The complex interaction between dietary fiber, transit time, and the frequency of bowel movements must also play a part in modifying the response of the colonic epithelium to continuous assaults by fecal mutagens. The protective mechanisms would operate within certain upper limits, which, if exceeded, would be expected to allow reversible or irreversible damage to occur to molecular and cellular components of the mucosa. (58 Refs)

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Diagnosis, Treatment

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THE DETECTION AND DIAGNOSIS OF COLONIC AND RECTAL NEOPLASMS

1. COMPARISON OF RIGID AND FLEXIBLE FIBREOPTIC SIGMOIDOSCOPY WITH DOUBLE CONTRAST BARIUM ENEMAS.

Vellacott KD, Amar SS, Hardcastle JD
Royal Devon and Exeter Hosp. (Wonford), Barrack Road, Exeter EX2 5DW, England
Br J Surg; 69(7):399-400 1982

One hundred consecutive new patients attending a general surgical and gastrointestinal outpatient clinic had a flexible fiberoptic sigmoidoscopic examination before a double contrast barium enema. Colonic lesions were found in 45 patients and flexible sigmoidoscopy was superior to barium enemas in diagnosing lesions in the sigmoid colon. Two cancers, one histologically a Dukes' A lesion, and six adenomatous polyps greater than 0.5 cm in diameter, in the sigmoid colon, were not detected by enemas. In six of these patients extensive diverticular disease was present. In patients with rectal bleeding found to have diverticular disease demonstrated radiographically, an endoscopic examination must be performed to exclude polyps or

HE20.3173/2:

cancer. Flexible fiberoptic sigmoidoscopy may reduce the numbers needing barium enemas. (Author abstract) (6 Refs)

2. DISTRIBUTION OF MALIGNANT POLYPS IN THE COLON.

Appel MF
Dept. General and Thoracic Surgery, Kelsey-Seybold Clinic, 6624 Fannin, Houston, TX, 77030
Dis Colon Rectum; 25(5):427-428 1982

The purpose of this study was to investigate whether the distribution of malignant polyps of the colon is the same as the distribution of all polyps in general. A consecutive and unselected series of 1,226 endoscopically removed polyps was analyzed; the analysis indicated strong preponderance of malignant polyps to be located in the left side of the colon. Ninety-five percent of the malignant polyps were taken distal to the splenic flexure, whereas that segment of the colon produced only 72% of all of the polyps in general. It is not possible to determine the reason for this from the present study, but the importance of removing these polypoid lesions continues to be emphasized by these data. (Author abstract) (4 Refs)

3. LOCALIZATION OF I-131-LABELED GOAT AND PRIMATE ANTI-CARCINOEMBRYONIC ANTIGEN (CEA) ANTIBODIES IN PATIENTS WITH CANCER.

Sullivan DC, Silva JS, Cox CE, Haagensen DE, Harris CC, Briner WH, Wells SA
Duke Univ. Medical Center, Box 3808, Durham, NC, 27710
Invest Radiol; 17(4):350-355 1982

Thirty patients with anti-carcinoembryonic antigen (CEA)-producing cancers of the colon, breast, or thyroid were injected with 1 to 2 mCi of 131I-labeled, affinity-purified, goat or baboon anti-CEA antibodies. Images were obtained daily for four days. Computerized background subtraction using 99mTc-labeled compounds was used. Images obtained with and without background subtraction were correlated with other evidence of disease. Activity levels in plasma, urine, and thyroid gland were monitored. Significant deiodination of antibody occurred within the first 24 hr. The mean plasma half-disappearance-time of baboon antibody was significantly longer than the mean half-disappearance-time of goat antibody. With exogenous blockade, total thyroid uptake was less than 0.1% of the injected dose. Without background subtraction, scintigraphic localization of known tumor was possible in one of two patients with colon carcinoma, in three of 20 patients with breast cancer, and in none of five patients with medullary carcinoma of the thyroid. With background subtraction, potential false-positive results could be generated for every patient, depending on the normalization site chosen and the degree of subtraction used. In contrast to results of previous reports, CEA-producing tumor was found to be infrequently localized using highly purified goat or primate radiolabeled anti-CEA. Furthermore, the subtraction technique described by previous investigators may lead to a high false-positive rate. (Author abstract) (7 Refs)

4. CONTRIBUTION OF THE PATHOLOGIST TO THE RADIOLOGY AND MANAGEMENT OF COLORECTAL POLYPS.

Morson BC, Konishi F
Dept. Pathology, St. Mark's Hosp., City Road, London EC1V 2PS, England
Gastrointest Radiol; 7(3):275-281 1982

Pathological characteristics of polyps and their potential for malignant transformation are discussed. Polyps with significant malignant potential are considered to be neoplastic. Neoplasia includes both adenomas and carcinomas. Colorectal adenomas are well-demarcated, circumscribed lumps of epithelial dysplasia with or without a stalk which may be categorized as tubular, tubulovillous, and villous. Patients at increased risk of colorectal cancer include those with a long history of extensive ulcerative colitis, members of polyposis coli and colorectal cancer families, those who have had colorectal cancer removed, and those with isolated adenomas. The role of colonoscopy in the diagnosis and evaluation of adenomas is described. The distribution and size of 1,187 colorectal adenomas is discussed with respect to site and grade of dysplasia, histologic types (81% tubular, 16% tubulovillous, and 3% villous), grade of dysplasia and histologic type, size and grade of dysplasia, and multiplicity of adenomas. The incidence of adenomas in colorectal cancer families and in metachronous cancer cases is described. (28 Refs)

5. COLORECTAL CANCER: EARLY DIAGNOSIS AND DETECTION.

Hardcastle JD, Vellacott KD
Dept. Surgery, Queens Medical Center, Univ. Nottingham, Nottingham NG7 2UH, England
Recent Results Cancer Res; 83:86-100 1982

The possible detection of asymptomatic colorectal tumors, resulting in an increase of the number of Dukes' stage A tumors found, is discussed. There is clinical, pathological, and epidemiological evidence to suggest that the majority of colorectal cancers arise from benign adenomatous polyps. The ideal screening test is sufficiently sensitive to detect most tumors without having a high false-positive rate. The only two practical methods at present are proctosigmoidoscopy and fecal occult blood testing. Approximately 42% of all colorectal cancers occur within range of the rigid sigmoidoscopy has shown a 3.2x greater yield of information with the flexible instrument. Preoperation with a single enema is adequate in over 90% of cases, and the examination takes only a few min longer than with the rigid instrument. Flexible sigmoidoscopy should probably be the first investigation of choice in patients found to be fecal occult blood-positive. Fecal occult blood testing, false negatives and hemoccult testing, immunological methods for early diagnosis of colorectal carcinoma, tumor-associated products in feces, and tumor markers in blood are among other topics discussed. (109 Refs)

6. THE CLINICAL STAGING OF RECTAL CANCER.

Nicholls RJ, Mason AY, Morson BC, Dixon AK, Fry IK
St. Mark's Hosp., City Road, London EC1, England
Br J Surg; 69(7):404-409 1982

The ability of rectal digital examination to recognize significant stages of local extent and lymph node involvement in adenocarcinoma of the lower two-thirds of the rectum was investigated. Seventy patients with a palpable rectal cancer were examined by 2 or 3 out of a panel of 10 clinicians including 2 consultants and 8 registrars. A defined protocol was used and the results were recorded on a proforma. Clinical findings were compared with the results of pathological examination of the resected specimen or the final surgical assessment when the growth was not removed. In 38 patients computed tomography of the primary growth was performed and the results were also compared to the pathological findings. Four groups of cases with different degrees of extent of spread were recognized by digital examination in 67-83% by consultants and in 44-78% by registrars. Computed tomography correctly identified growths with extensive local spread in 89% of cases, but was no more reliable than digital examination in the assessment of other degrees of spread or of lymph node involvement. Based on the results, a clinical staging system is proposed, comprising four Stages of local extent as follows - Stage 1: confined to rectum; Stage 2: confined to rectum or slight extrarectal spread; Stage 3: moderate or extensive extrarectal spread; Stage 4: involvement of other organs or unresectability. Two stages of lymph node involvement are also proposed: namely, node negative and node positive. Each stage corresponds to different survival and local recurrence rates after surgery. Combined with other factors, such as level and size of tumor, histological grade and the general state of the patient, the clinical staging system may facilitate the choice of treatment. It might extend the use of major sphincter-saving procedures, identify many patients suitable for local treatment and define those with a considerable risk of local recurrence where combined surgery and radiotherapy might be considered. (Author abstract) (5 Refs)

7. COMPARATIVE STUDY OF FAMILIAL POLYPOSIS COLI AND NONPOLYPOSIS COLI ON THE HISTOGENESIS OF LARGE-INTESTINAL ADENOMA.

Oohara T, Ihara O, Saji K, Tohma H
Third Dept. Surgery, Univ. Tokyo, 3-28-6 Mejirodai, Bunkyo-ku, Tokyo 112, Japan
Dis Colon Rectum; 25(5):446-453 1982

The entire length of the large intestine resected from six patients with familial polyposis coli (FPC) was step-sectioned, and microscopic adenomas composed of one to several glands were prepared into complete serial sections. Histopathologic comparison of these microscopic adenomas was made between FPC and nonpolyposis coli (those not included in the special disease group of FPC). The histogenesis of adenomas in FPC and nonpolyposis coli was considered as follows. (1) In nonpolyposis coli, adenomas arise from basal cells of the deep layer of the mucosa. (2) In FPC, most of the adenomas (81.2%) arise in the same manner as described above, although there are some (18.8%) that appear to have arisen in the middle or superficial layer of the mucosa. (3) Therefore, it is believed that the morphologic difference of the large-intestinal mucosa between FPC and nonpolyposis coli comes not from the difference in the number of adenomas present but from the difference in the position and/or timing of appearance of adenomas. (Author abstract) (21 Refs)

8. ENDOCRINE CELLS AND MELANIN-CONTAINING CELLS IN THE ANAL CANAL EPITHELIUM.

Fenger C, Lyon H
Univ. Dept. Pathology, Odense Sygehus, DK-5000 Odense C, Denmark
Histochem J; 14(4):631-639 1982

The epithelium of the anal canal was studied by histochemical methods to determine the presence of endocrine and melanin-containing cells. Tissue was obtained from 22 patients who underwent abdominoperineal resection of colorectal adenocarcinomas. Fifteen of the tumors were located above the dentate line. The tissue examined contained normal anal transitional zone (ATZ) tissue and adjoining colorectal and squamous tissue. Colorectal crypts were found in and proximal to the ATZ in all 22 specimens. Colorectal epithelium contained goblet cells, demonstrated by aldehyde-fuchsin stain, and endocrine cells, indicated by argyrophilia and the presence of biogenic amines. No melanin-containing cells were found in the colorectal epithelium. ATZ epithelium was found in all 22 specimens. Mucous substances were found on the luminal surfaces of columnar cells and in goblet cells. Areas of cuboidal or flattened cells showed no mucous substance. Endocrine cells were found in 19/22 specimens of ATZ epithelium; melanin-containing cells were found in two specimens. Anal glands were found in 10 specimens; mucous substances were found in 10 cases and endocrine cells in 8; no melanin was observed. Squamous epithelium was found distal to the dentate line in all cases and proximal to the line as scattered islands in approx 50% of the cases. Squamous epithelium showed no endocrine cells. Melanin-containing cells were found, with numbers increasing with proximity to the anal margin. The presence of endocrine cells in the anal canal suggests the canal as a possible origin of carcinoids. The presence of melanin-containing cells may explain the occurrence of melanomas above the dentate line. (28 Refs)

9. CARCINOEMBRYONIC ANTIGEN. PHYSICIAN ATTITUDES, PATTERNS OF USE, AND IMPACT UPON PATIENT CARE.

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Dig Dis Sci; 27(4):289-296 1982

Recent data would limit indications for serum CEA measurement primarily to follow-up of resected colonic malignancy, yet physician attitude and usage patterns may lag far behind current findings. This discrepancy was investigated at our institution, where more than 1100 CEAs costing 71,000 dollars are ordered each year. Of 45 physicians (all MDs ordering a CEA test during a preselected month), over 50% believed the test to be worthwhile in initial detection of colonic cancer, and 69% thought an elevated CEA to be an adequate reason to begin an aggressive workup to rule out cancer of the colon in a nonsmoking, previously healthy patient. Impressions of cost were less than or equal to 30 dollars (50% of true cost) in nearly half of MDs and less than or equal to 20% of true cost in a tenth of MDs. Analysis of the medical record revealed that indications of questionable validity (initial detection of cancer together with follow-up of noncolonic malignancy) accounted for the majority of requested CEAs and included the attempted detection or monitoring of 12 different tumor types in addition to its use as a 'general cancer screen.' Patient benefit was realized in none in a random sample of 106 cases (beta = 0.11, power = 0.89 for an assumed benefit of 2%), while management was altered in only one patient as a direct result of the CEA value. It is important that we continue to inform and educate our colleagues about relatively expensive tests that have only limited and specific application. (Author abstract) (29 Refs)

10. CEA MONITORING AMONG PATIENTS IN MULTI-INSTITUTIONAL ADJUVANT G.I. THERAPY PROTOCOLS.

Steele G, Ellenberg S, Ramming K, O'Connell M, Moertel C, Lessner H, Bruckner H, Horton J, Schein P, Zamcheck N, Novak J, Holyoke ED
Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Ann Surg; 196(2):162-169 1982

The Gastrointestinal Tumor Study Group (GITSG) has since 1975 included protocols for monitoring carcinoembryonic antigen (CEA) levels in its colorectal cancer adjuvant trials. Among the 563 patients on the colon cancer study (GI 6175) and the 207 patients on the rectal cancer study (GI 7175), one third had preoperative CEA determinations and more than

90% had some postoperative CEA monitoring. Colon cancer patients whose preoperative CEA was greater than 5 ng/ml had a greater probability of recurring than those whose values were lower. The prognostic value of preoperative CEA was apparent only in patients with Dukes' C1 colon tumors. Preoperative CEA values were not of prognostic significance among the rectal adenocarcinoma patients. Although elevated levels of CEA after resection of either colon or rectum cancers were strongly associated with subsequent tumor recurrence, no single CEA value, arbitrarily defined as 'elevated', provided an adequate screening test with both high sensitivity and high specificity. Postoperative CEA elevations were more strongly predictive of recurrence when part of a steadily rising trend. Only 36 of the 344 disease-free patients on the colon protocol and 14 of the 94 disease-free patients on the rectal protocol (15%) exhibited a rate of increase of CEA as high as 3% per month over the entire period of observation. Two thirds of the relapsed patients on both studies showed a high rate of increase. The patterns of CEA rise in individual patients were quite varied, however, and monthly rates of increase as established in our study are not to be used as guidelines in patient management. (16 Refs)

11. SERUM GLYCOSYL TRANSFERASES AND CARCINOEMBRYONIC ANTIGEN IN PATIENTS WITH COLORECTAL CARCINOMA IN DIFFERENT STAGES.

Ronquist G, Rimsten A, Blanche C, Cerven E, Hiesche C, Westman M
Dept. Clinical Chemistry, Univ. Hosp., Uppsala, Sweden
Acta Chir Scand; 148(4):373-377 1982

Serum samples from 170 patients were investigated with regard to sialyl- and fucosyltransferase activities as well as CEA (carcinoembryonic antigen) content. These patients constituted three different groups, the first consisting of 80 patients with colorectal carcinoma, primary or recurrent. The second group consisted of 32 patients with earlier treated colorectal carcinoma and with no evidence of recurrence. For comparison a third group was selected consisting of 58 patients with benign surgical disease. The sialyl- and fucosyltransferase activities as well as CEA content were significantly (p less than 0.001) elevated in patients with colorectal carcinoma, primary or recurrent, when compared to the patients with benign surgical disease. When comparing the former patients with those having earlier treated colorectal carcinoma but with no evidence of recurrence a more complex pattern was present. Thus there were significantly (p less than 0.001) lowered CEA values among the latter patients as determined by two different methods while at the same time an increase (p less than 0.05) in fucosyltransferase activity and an unaltered sialytransferase activity were apparent. The patients with colorectal carcinoma were also subgrouped, A-D with regard to cancer spread. Subgroup A represented a cancer localized to the mucosa while Subgroup D included those with known distant metastases. Intergroup comparisons revealed no significant differences between the various subgroups as regards sialyl- and fucosyltransferase activities. The highest mean value for sialyl transferase was found in Subgroup A. Although significant differences existed for both glycosyltransferases and CEA between the patients with malignant and benign diseases a great deal of overlapping occurred between the groups. Furthermore, these different analyses did not essentially reinforce each other in diagnostic sharpness. Therefore, these biochemical tests when combined were not sufficient to categorize the patients in two groups namely those with colorectal carcinoma and those with benign surgical disease. (Author abstract) (10 Refs)

12. COLORECTAL CANCER: BIOCHEMICAL MARKERS.

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Unit for Cancer Res., Univ. Leeds, Leeds LS2 9NL, England
Recent Results Cancer Res; 83:67-76 1982

The contribution of pre- and post-operative measurements of carcinoembryonic antigen (CEA), gamma glutamyl transferase (gGT), and CEA measured by the Laurence assay to survival were evaluated in 145 patients with colorectal cancer. Median age of the patients was 66 yr (79 males, 66 females). Dukes' A or B lesions accounted for 49% (71 patients), C lesions for 32% (47 patients), metastatic disease at the time of surgery (stage D) for 19% (27 patients). Within a given Dukes' stage, survival varied considerably according to pre-operative CEA and gGT levels and according to the extent to which they changed after surgery. Pre-operative CEA levels carried prognostic information supplementary to Dukes' stage. Variation of CEA in post-operative patients was small about each individual's own mean, but levels of 1-6 nanog/ml (ng/ml) were all compatible with health. Median level of CEA in advanced colorectal cancer rose as patients approached death, but variability remained very large. In 24 patients with advanced cancer who were first seen with an initial CEA level that was greater than 5 ng/ml but less than 20 ng/ml the median survival was 7 mo, while the 37 patients with initial CEA greater than 20 ng/ml median survival was 4 mo. In patients with advanced colorectal cancer, acute phase reactant proteins were found to be normal in 69% of patients 6-12 mo prior to death, moderately increased in 16%, and markedly increased in 16%. (17 Refs)

13. MEASUREMENT OF SERUM FERRITIN IN VARIOUS DIGESTIVE DISEASES BY REVERSED PASSIVE HEMAGGLUTINATION USING ANTI-HUMAN PLACENTAL FERRITIN ANTISERUM.

Tomoda H, Furusawa M, Seo Y, Matsukuchi T, Miyazaki M, Kanashima R
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Jpn J Clin Oncol; 12(1):9-16 1982

Serum ferritin values were determined in 226 cases of various digestive diseases with the aid of anti-human placental ferritin antiserum used to provoke reversed passive hemagglutination, and the utility and limitations of the method were studied. Effects of combining serum ferritin assays with those for blood carcinoembryonic antigen (CEA) or serum alpha-fetoprotein (AFP) were also studied with respect to improving cancer diagnosis. The diseases included 30 benign diseases, 170 malignant diseases, and 26 recurrent diseases. Compared to the frequency of abnormal serum ferritin values among cases of benign diseases (10%), those for recurrent gastric cancer (44.4%), recurrent colorectal cancer (55.8%), pancreatic cancer (50%), and primary hepatoma (66.7%) were significantly higher. Compared to the cases of benign disease, cases of primary colorectal, esophageal, and pancreatic cancers and primary hepatoma had significantly higher frequency of abnormal values of either or both serum ferritin and blood CEA; rates of abnormal values in cases of recurrent colorectal and gastric cancer were significantly higher than in cases of primary colorectal and gastric cancer. Compared to the assay of serum ferritin alone, the combination assay for serum ferritin and serum AFP showed a higher incidence of abnormal values. The combination assays were thought to be useful for supplemental diagnosis of cancer. (23 Refs)

14. ANOMALOUS EXPRESSION OF HLA-DR ANTIGENS ON HUMAN COLORECTAL CANCER CELLS.

Daar AS, Fuggle SV, Ting A, Fabre JW
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J Immunol; 129(2):447-449 1982

Expression of HLA-DR and HLA-ABC antigens was examined in 15 colorectal cancer specimens. All samples of normal colon and rectum were taken from surgical resection specimens from areas distant from the tumors. Two patterns of HLA-DR positivity were observed in the tumor specimens. One pattern exhibited isolated positive cells with malignant cells clearly not staining. In the second pattern an apparently relatively well-differentiated crypt but with intensely HLA-DR-positive epithelium was observed in the longitudinal section. It could not be established whether the observed pattern represented malignant cells attempting to differentiate into normal but HLA-DR-positive epithelial crypts or the induction of HLA-DR antigens in a normal crypt in close contact with the tumor. Of the 15 tumors examined, 8 had patches of HLA-DR-positive malignant cells as observed in the first pattern. No correlation could be seen with degree of differentiation of the tumor, its site of origin, or degree of leukocytic infiltration. Fourteen of the 15 tumors were positive throughout for HLA-ABC antigens. In a very poorly differentiated adenocarcinoma, the staining was obviously weaker, and approx one-half of the tumor mass did no stain at all. The findings might define a biologically important heterogeneity among populations of tumor cells. (17 Refs)

15. IMMUNOHISTOCHEMICAL TECHNIQUES IN THE EARLY SCREENING OF MONOCLONAL ANTIBODIES TO HUMAN COLONIC EPITHELIUM.

Finan PJ, Grant RM, De Mattos C, Takei F, Berry PJ, Lennox ES, Bleehen NM
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Br J Cancer; 46(1):9-17 1982

Selected monoclonal antibodies (McAbs) isolated after immunization of rats with a human colonic carcinoma membrane preparation, have been screened on frozen and paraffin sections of colonic tissue, using immunohistochemical techniques, in order to provide additional information with regard to specificity and cross-reactivity with normal tissues. Of 10 McAbs previously shown to bind to a colonic carcinoma membrane preparation in a radioimmunoassay, 7 show specific staining when tested by indirect immunofluorescence on cryostat sections of colonic tissue. Three of these seven show activity on both normal and malignant colonic epithelium, and the remaining four stain normal epithelium, with little or no activity on malignant tissue. In the indirect immunofluorescent and immunoperoxidase techniques on paraffin sections of the same material, only two McAbs retain activity; one detects an antigen in colonic mucus, and the other recognizes an antigen which is sparse on normal colonic epithelium and abundant on colonic tumors. We conclude that screening of McAbs on frozen tissue sections, using indirect immunofluorescence, is a useful adjunct to conventional screening methods, eg binding to membrane preparations and/or cell lines in a radioimmunoassay. These techniques distinguish McAbs with similar binding values in conventional assays, identify their activity on a wide range of normal and malignant tissues, demonstrate antigens that are lost or gained in malignant transformation and finally assist in the selection of McAbs for further extensive study before possible clinical use. (Author abstract) (15 Refs)

16. CYTOTOXICITY OF CANCER PATIENT'S MACROPHAGES FOR TUMOR CELLS.

Cameron DJ, O'Brien P
Dept. Surgery, Medical Univ. South Carolina, 171 Ashley Ave., Charleston, SC, 29403
Cancer; 50(3):498-502 1982

Monocyte derived macrophages were isolated from the peripheral blood of 66 patients with either breast, colon, gynecological or hematological cancers. The macrophages from the breast and gynecologic cancer patients generally did not acquire enhanced cytotoxicity for human tumor cells after incubation with bacterial lipopolysaccharide (LPS). However, when the macrophages isolated from colon and hematologic cancer patients were studied, more than 50% of these patients possessed cytotoxic macrophages. LPS induced macrophage mediated cytotoxicity was also found to be inhibited by factors present in many cancer patient's plasma. Twenty-three of the 50 cancer patients studied possessed a plasma inhibitor capable of suppressing macrophage mediated cytotoxicity by more than 50%. Furthermore, of these 50 patients, 47 were incapable of killing the tumor cells in vitro either because they possessed nonresponsive macrophages and/or they possessed a plasma inhibitory factor. Thus, although macrophage cytotoxic function may be normal in some patients with cancer, cytotoxicity may be inhibited in some patients by factors in autologous plasma thereby rendering the macrophages ineffective in vivo. (Author abstract) (10 Refs)

17. STUDY ON T-CELLS BEARING FC RECEPTORS FOR IGG IN PATIENTS WITH CANCER OF DIGESTIVE ORGANS.

Taki M
Dept. Surgery, Okayama Univ. Medical Sch., Okayama, Japan
Nippon Gan Chiryo Gakkai Shi; 17(3):720-727 1982

T- and Tgamma-cell populations were measured in 23 healthy controls, 9 controls with benign diseases, and 68 patients with gastrointestinal cancers (46 gastric, 16 rectal, 3 esophageal, and 3 pancreatic), and the relationships of the Tgamma-cell populations to other immunological parameters were studied. Also, the antibody-dependent cellular cytotoxicity (ADCC) and natural killer (NK) activities of various fractions of peripheral lymphocytes were determined. Tgamma-cells were detected with the aid of double-rosette forming method using non-coated sheep RBC and rabbit IgG antibody-coated chicken RBC. Tgamma-cell percentages were higher in the patients with cancer than in the controls. Compared to that of controls (5.4 +-2.1%), percentages of Tgamma-cells were 4.7 +-2.2% in patients with Stage I gastric cancer, 5.9 +-2.7% in Stage II, 8.5 +-3.9% in Stage III, and 8.7 +-4.4% in Stage IV. Percentages of Tgamma-cells increased with respect to increased Stage of the cancers, and the percentages returned to within the normal range when tumors were extirpated. ADCC and NK activities of the fractions of lymphocytes were highest in the Tgamma-rich fractions, and decreased in the order of T-rich, B-rich, and T non-gamma-rich fractions. No differences in the activities of each fraction were observed between the lymphocytes from the controls and cancer patients. (16 Refs) (In JPN)

18. THOUGHTS ON AND PROGRESS IN DIAGNOSIS OF LARGE INTESTINE DISEASES: OCCULT BLOOD REACTION AND CLINICAL SYMPTOMS.

Ichikawa H, Nakajima H, Muto T, Ushio K, Watanabe H
Natl. Cancer Center Hosp., Tokyo, Japan
I To Cho; 17(4):465-470 1982

Various aspects and techniques of diagnosing large intestinal diseases are discussed. Topics included the necessity of using the 3-day occult blood test vs the 1-day test, the possibility of not discovering colon cancer in spite of combining various intestinal examination methods, features of colon cancer which distinguish it from inflammatory bowel disease, counterindications to use of enhanced roentgenography or fiberscopy, and the limits of examining patients with chronic occult blood. (no Refs) (In JPN)

THERAPEUTIC MODES OF COLO-RECTAL CANCER TREATMENT

19. LOCAL, TRANSANAL, CURATIVE TUMOR RESECTION IN LOW RECTAL CANCER.

Scheele C, Reichel K
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Chirurg; 53(6):393-395 1982

Twenty-two patients (av age 66 yr) with low rectal cancers were treated by local, curative transanal tumor resection (TTR). No postoperative deaths occurred. Two patients died of other diseases 2.5 and 5 yr after surgery. No patients developed scarring stenosis or incontinence. TTR is recommended for certain carefully chosen patients who meet criteria for tumor characteristics and patient condition. Regular follow-up digital and endoscopic examinations are required. (7 Refs) (In GER)

20. COLORECTAL CANCER: SURGERY.

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Recent Results Cancer Res; 83:101-112 1982

Surgery remains the treatment of choice for patients with colorectal carcinoma, and the only therapy offering the possibility of cure at the present time. However, survival after surgical removal of both rectal and colonic carcinomas has not improved during the last 30 yr. The overall 5-yr-survival of 248 patients treated by conservative surgeons (based on the extent of resection normally carried out) was 35%, in contrast to 47% of 323 patients treated by aggressive surgeons. This difference was almost completely accounted for by the difference in the number of patients whose cancer was not resected. The survival of patients with resected growths was around 40% whether treated by the conservative or the aggressive surgeons, indicating that an improved survival rate can be obtained by increasing the resectability rate. There is some evidence that extent of mesenteric clearance is important for survival, but little is gained by extensive pelvic lymphatic removal in rectal carcinoma. Sphincter-preserving operations (including local excision) for correctly selected tumors are as likely as total rectal excision to result in long-term survival. Surgery for metastatic disease or local recurrence results in a certain number of long-term survivors, but these form only a small fraction of the total number of patients with advanced disease. (39 Refs)

21. COLORECTAL CARCINOMA - TRENDS AND RESULTS OVER A 30-YEAR PERIOD.

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Dis Colon Rectum; 25(5):431-440 1982

The experience of Karolinska Hospital with colorectal carcinoma over a 30-yr period, 1950 through 1979, was reviewed and analyzed. Altogether, 1,061 patients were seen; 69% were resected with the intention of cure. The proportion of curative resections did not change with time. Operative mortality decreased from 12 to slightly over 1%. Five-year survival rates were 34% overall and 47% in curable cases. After correction for operative mortality, the latter rate increased from 47 to 58% over the study period (no significance). Sex and age were not correlated with survival. Of tumors resected for cure, 28% were Dukes' A, 39% Dukes' B, and 33% Dukes' C. Corresponding 5-yr survival rates were 82, 44, and 21%. Though the proportion of Dukes' A tumors increased from 23 to 33% over the 30-year interval, the impact on overall prognosis was insignificant. A possible overdiagnosis of Dukes' A is discussed. The proportion of sphincter-saving procedures for rectal carcinoma increased moderately; excisional and restorative procedures were equal with respect to mortality and survival. Some patients underwent local excisions for Dukes' A rectal carcinomas with a close to 90% 5-yr survival. (Author abstract) (56 Refs)

22. PRIMARY CLOSURE OF THE PERINEUM FOLLOWING ABDOMINAL PERINEAL RESECTION OF THE RECTUM FOR CARCINOMA.

Delpero JR, Le Treut Y, Boutboul R, Bricot R
Clinique Chirurgicale de l'Hotel-Dieu, 6, place Daviel, F 13224 Marseille, France
J Chir (Paris); 119(5):375-380 1982

Rectal cancer resection was performed in 105 cases (51 men and 54 women). In men wide resection was necessary in only six cases whereas in women it was necessary in 30 cases. Surgery with curative intent was performed in 80 cases whereas in 25 cases, palliative surgery was performed. Operative mortality was 7.6% (8/105). Four pliable drains were inserted following surgery. Primary wound healing was obtained in 81 patients (77.2%) or in 82.3% of the men and in 72.2% of the women. In five cases, there was total disunion of the wound. In 14 cases, partial disunion occurred, and in five cases, there was infection of the surgical cavity without wound disunion. Women were affected by partial disunion in 12/14 cases, and all cases of infection involved men. The palliative vs curative intent of the surgery and the method of drainage did not have any significant effect on healing. Conditions which were identified as having an effect on healing included hemostasis, asepsis, peritonization, and enlargement followed with ablation of the genital tract in women. (15 Refs) (In FRE)

23. BOWEL FUNCTION FOLLOWING ANTERIOR RESECTION WITH STAPLED ANASTOMOSIS (MEETING ABSTRACT).

McDonald PJ, Heald RJ
Department of Surgery, Basingstoke District Hospital, Basingstoke, England
British Association of Surgical Oncology Summer Meeting, July 15-16, 1982, Portsmouth, England British Association of Surgical Oncology; 1982

The assumption that removal of all or most of the rectum leads to an incontinent perineal colostomy, is still used as a justification for abdominoperineal excision. It is likely that many patients continue to undergo the latter operation when their rectal cancers could be radically resected with a sphincter-saving procedure. We have studied 75 patients, who had previously had a sigmoid colectomy or an anterior resection using a stapling device. These patients were assessed for bowel function and classified into three groups depending on the distance of the anastomosis from the anal verge: group A greater than 10 cm; group B 5-10 cm; group C less than 5cm. An age-matched control group of patients attending a general surgical clinic was assessed similarly. The following facts about their bowel habit were noted: previous frequency and control; immediate postoperative control; present frequency of defecation; ability to discriminate wind from feces; ability to defer defecation for more than 15 minutes; need to wear pad or minor leakage and need to modify diet due to bowel habit. A continence scale was defined: I - perfect control; II- change in hibit (usually an increase in frequency that does not affect lifestyle); III - increased frequency that interferes with lifestyle, or slight soiling or need to wear a pad; IV - occasional day or night-time incontinence; V - total incontinence. The median follow-up time for the patients was: A equals 20.5 months (range 3-34); B equals 19.5 months (3-31) and C equals 16.0 months (5-28). The difference in function between groups A and C was statistically significantly poorer for group C. Similarly, the different continent 'score' between groups A and C was highly significantly different with no patients in group A and 8/21 (38%) of patients in group C scoring III. Differences between group B and C reached statistical significance for delay and the pad or soiling group. Two patients (one in Group B and one in group C) required colostomies due to uncontrollable incontinence. The control group did not have perfect function and was similar to group A. (no Refs)

24. SPHINCTER-SAVING RESECTION OF THE RECTUM USING THE EEA AUTOSTAPLER.

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Dept. Surgical Gastroenterology C, Rigshospitalet, Univ. Hosp., Copenhagen, Denmark
Acta Chir Scand; 148(4):379-381 1982

Low anterior resection for carcinoma in the mid- and lower third of the rectum has been performed with autosuture technique, using the EEA autosuture stapling instrument in 38 patients, 26 with carcinoma, 10 with diverticulitis, and 2 with Crohn's disease. In 16 patients the anastomotic line was 4-6 cm above the anal verge, and in 22 patients 7-12 cm above the anal verge. Thirty-two patients (80%) had an uneventful postoperative course. Four patients had complications: one, with leakage from a very low-seated anastomosis, was treated with an abdominoperineal resection; two had temporary transversostomy performed due to minor anastomotic leakage; and one patient developed a fistula, which closed spontaneously. Two patients died, one from pulmonary embolism, one from cerebral thrombosis. The EEA stapling instrument seems safe, and approx 42% of the patients in this material would formerly have been subjected to abdominoperineal resection and permanent colostomy. (Author abstract) (9 Refs)

25. PREOPERATIVE RADIATION THERAPY FOR RECTAL CARCINOMA.

Roe JP, Kodner IJ, Walz B, Fry RD
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Dis Colon Rectum; 25(5):471-473 1982

Preoperative irradiation was given to 58 selected patients with adenocarcinoma of the rectum to decrease local recurrence and to improve survival. The irradiation was well tolerated without increasing operative complications. At a median follow-up of 25 months, the local failure rate appeared to be improved. Evaluation of increased length of survival will require longer follow-up. Results suggest that preoperative irradiation can safely decrease local recurrence of rectal carcinoma in patients believed to be at higher risk for local recurrence. (Author abstract) (14 Refs)

26. COLORECTAL ADENOCARCINOMA: RESULTS WITH POSTOPERATIVE RADIATION (MEETING ABSTRACT).

Moore MJ, Heusinkveld RS
Division of Radiation Oncology, University of Arizona Health Sciences Center, Tucson, AZ, 85724
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1973 and 1980, 61 patients received postoperative radiotherapy following curative resection of a colorectal adenocarcinoma. In 54 patients the surgical resection had been the initial treatment; in 7/61 patients postoperative radiotherapy was given following total excision of carcinoma recurrent at the site of previous resection. No patient had evidence of distant metastatic disease. Patients were staged using the modification of the Astler-Coller system described by Gunderson and Sosin. Twenty-three patients had Stage B2, 9 patients - B3, 1 patient - C1, 13 patients - C2 and 7 patients - C3. There were 7 patients with recurrent tumors. Patients were treated with a 4 or 10 MeV Linear Accelerator using a 2-field (AP-PA; anteroposterior-posteroanterior opposed), 3 field (posterior and 2 lateral fields), or 4-field technique. Seventy-three percent of patients received a total of 5000 to 5500 rad in 6 weeks. The perineum was included for part of the treatment if an AP resection had been performed. With a median follow-up of 30 months, 54% of patients were alive NED (no evidence of disease). Local failure in the treated volume, with or without distance metastases, has occurred in 22% of the entire series; 9% with Stage B2, 44% with B3, 0/1 with C1, 15% with C2 and 60% with C3 lesions. Three out of seven patients with recurrent lesions are NED with only 1 of 7 having had a local recurrence. Two out of sixty-one patients have had serious complications, one patient developing rectal stenosis at the anastomotic suture line. A second patient developed a small bowel obstruction due to adhesions in the pelvis. Treatment results with B2 and possibly C2 lesions, thus far, have been satisfactory. Tumor dose may be inadequate in more advanced lesions where more than minimal microscopic disease could remain. (no Refs)

27. PREOPERATIVE RADIOTHERAPY IN RECTAL ADENOCARCINOMA (MEETING ABSTRACT).

Lopes da Conceicao A, Cox JD, Byhardt R
Radiation Oncology Department, Mount Sinai Medical Center, Milwaukee, WI
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Preoperative megavoltage external pelvic irradiation was given to 30 patients with the confirmed histological diagnosis of adenocarcinoma of the sigmoid rectum, 12 female, 18 male, age range 26-85 years, median age 63 years. The external radiation with megavoltage was delivered mostly through AP and PA parallel opposing portals to the whole pelvis (portals about 15 x 15 cm) and the doses used at midplane were about 4500 rads, 180-200 rads/day/5 x week, for about one-half of the patients and 5000 rads, 180-200 rads/day/5 x week for the other one-half. Surgery was performed for the majority of the patients between 4 and 6 weeks after the completion of the radiotherapy program. The operative procedures performed were AP resections in 20 cases and low anterior resections in 10 cases. Two patients revealed liver mets (metastases) at laparotomy but no other cases of dissemination were detected during first surgery. Eighteen patients are surviving NED (no evidence of disease), 4 patients between 6 and 9 months after Dx (diagnosis), 3 patients between 1 1/2 and 2 years, and 11 between 2 1/2 and 6 1/4 years. Three patients are alive with mets in 2 and pelvic recurrence in one, at 10 months, 17 months and 26 months, respectively. Nine patients died between 9 months and 64 months all with distant mets and only 3 with pelvic recurrences. Altogether the number of pelvic recurrences were 3/30 or approx 10% in these advanced rectal tumor patients and 40% of the patients developed distant mets found at first surgery or within 3 years after Dx. Evidence of pelvic recurrences occurred between 2 years and 2 years, 8 months after Dx. (no Refs)

28. RADIATION THERAPY OF COLORECTAL CANCER (MEETING ABSTRACT).

Gunderson LL
Mayo Clinic, Rochester, MN
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

The combined modality approach for initial treatment of rectal and selected colonic carcinomas is based on 1) data that 'radical' operations do not necessarily prevent either local regrowth or failures in the tumor bed and regional lymph nodes or distant failures via hematogenous or peritoneal routes; 2) acceptance of a significant palliative but infrequent curative role for irradiation and chemotherapy when such failures occur; and 3) acceptance of 'subclinical disease' radiation dose concept. Incidence and location of operative failures will be correlated with initial operative and pathologic extent of disease in reoperative and clinical series and increased emphasis will be placed on colonic cancer. Preliminary data for rectal and rectosigmoid cancer suggests that local recurrence can be markedly reduced by moderate to high dose pre- and post-operative irradiation, but distant metastases continue to be a problem. Therapeutic 'gains' achieved with irradiation might be offset by an increase in complications unless wisdom is used in treatment planning. Techniques to improve both tumor and normal tissue localization will be dovetailed with a discussion of optimization portals with shaped multiple fields and 'shrinking field' techniques. Future possibilities of irradiation, including tumor bed and/or whole abdominal or liver XRT for selected colonic lesions and intraoperative XRT will be discussed. (no Refs)

29. ADJUVANT POSTOPERATIVE RADIATION THERAPY FOR COLORECTAL CARCINOMA ABOVE THE PERITONEAL REFLECTION: I. SIGMOID COLON (MEETING ABSTRACT).

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Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

From 1970-1981, 85 patients had curative sigmoid resections for adenocarcinoma and were eligible for postoperative adjuvant therapy. In a non-randomized fashion, 10/28 B2,3 and 7/28 C2,3 patients received postoperative pelvic radiation therapy (4500-5100 rad/5-6 weeks). Compared to the 39 B2,3 or C2,3 patients not receiving adjuvant pelvic radiation therapy (4500-5100 rad/5-6 weeks). Compared to the 39 B2,3 or C2,3 patients not receiving adjuvant pelvic irradiation, those 17 who did demonstrated retrospectively an improved pelvic regional disease control rate (70%vs 91%) and an improved 5-year survival for irradiated B2,3 cases vs unirradiated B2,3 cases. (100% vs 64% P less than 0.05). C2,3 cases showed no survival advantage for pelvic irradiation. This retrospective analysis suggests that for sigmoid carcinoma patients, postoperative adjuvant pelvic irradiation may be beneficial in terms of improved regional disease control rates for B2,3 and C2,3 cases and also improved survival for B2,3 cases. (no Refs)

30. CLINICAL EXPERIENCE WITH RADIATION THERAPY FOR CARCINOMA OF THE RECTUM (MEETING ABSTRACT).

Derdel J, Mohiuddin M, Kramer S
Thomas Jefferson University Hospital, Philadelphia, PA, 19107
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

From 1975 to 1981, 349 patients with rectal cancer were treated with radiation therapy at Thomas Jefferson University Hospital. Forty-one of these patients were treated for palliation of symptoms, while the remainder were treated definitively, either with high dose radiation alone or in combination with surgery. All patients were treated with megavoltage equipment, using a four field box technique and treatment optimization wherever indicated. One hundred twenty-nine patients were treated with high dose radiation. All patients received a minimum of 5000 rads and a maximum of 7000 rads. Patients obtained excellent palliation of symptoms. Control of bleeding was obtained in 95% of patients and tenesmus was relieved in 70% of patients. However, only 65% of patients obtained significant relief from pain, and of these, only 22% had complete pain relief. Sustained local control in these patients also has been poor, with 23% of patients having long term control of disease greater than 2 years duration. Two hundred ten patients were treated with a combination of radiation therapy and surgery. Several approaches to adjuvant therapy were used. Sixty-five patients received low dose preoperative radiation (less than 1000 rads) alone, 49 patients received high dose preoperative radiation (greater than 4000 rads), 38 patients received combined pre and postoperative radiation, and 36 patients received postoperative radiation only. The radiotherapy treatment techniques and volumes in these four groups was very similar. A careful comparison of these groups of patients has been made to assess the impact of the different approaches to adjunctive radiation therapy on the control of cancer and survival of patients. (no Refs)

31. A PHASE I-II PILOT STUDY OF DELAYED SPLIT WHOLE ABDOMINAL IRRADIATION FOR COLORECTAL CARCINOMA (MEETING ABSTRACT).

Meek A, Order SE, Torres JP
Department of Radiation Oncology, The Johns Hopkins Hospital, Baltimore, MD, 21205
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

The 20 patients selected included completely resected postoperative pelvic and extra pelvic colorectal lesions at high risk for recurrence (B2, C1, C2) and cases with known residual intra-abdominal disease and/or liver metastases. Treatment was administered using an 80 cm isocentric Cobalt 60 Unit with two pairs of AP PA fields; the abdominal port covering the dome of the diaphragm down to the iliac crest (average size 35 cm wide x 25 cm high) and the pelvic port covering from the iliac crest to below the obtruator foramen (average size 18 cm wide x 20 cm high). A calculated gap separated the fields so that they met at mid plane. Six half value layer kidney blocks were used on the PA abdominal field. Both pairs of field were treated 4 days a week with a 2 hour delay between the pelvic fields (treated first), and the abdominal fields. In the majority of cases the abdominal field was treated to 3000 rad in 5 weeks, 150 rad daily fractions, and the pelvis to 4000 rad in the same time at 200 rad fractions. Commonly a boost field of 1000 rad in 5 days was applied to site at highest risk for recurrence or known residual disease. Treatment in general was well tolerated. Nausea and diarrhea were mild enough to be controlled with symptomatic medication. Weight loss was minimum to none in 13 patients with 7 patients losing between 5-10% of pretreatment weight. Hematopoietic toxicity was moderate with 7 patients requiring one to two week treatment breaks for recovery of counts. Leukopenia to less than 2000 occurred in one patient and 3 others had thrombocytopenia to less than 50,000, both without consequence. (no Refs)

32. PRIMARY RADIATION THERAPY IN THE MANAGEMENT OF ANAL CARCINOMA (MEETING ABSTRACT).

Cantril ST, Green JP, Schall G, Schaupp WC

St. Francis Hospital and Children's Hospital, San Francisco, CA

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Forty of the 47 patients were treated with radiation therapy to an intact anal canal. Only two patients received any chemotherapy, both for locally advanced disease. Thirty of the 40 patients were treated for localized (less than 5 cm) lesions, two with preoperative intent. Of the remaining 28 patients treated definitively with radiation therapy, 24 have maintained anal continence. One patient underwent colostomy for benign stricture of the anal canal, two patients underwent abdominal perineal resection for benign non-healing ulcers of the anal canal, and one underwent abdominal perineal resection for persistent disease. Twenty-five of the 30 localized disease patients remain alive without disease, 18 of whom have been followed for more than two years, and two died without disease from two months to eight years. An additional 10 of the 40 patients were treated for advanced lesions (greater than 5 cm) and four have maintained anal continence. Of the remaining six patients, one was treated with preoperative intent, four had abdominal perineal resections for persistent disease, and one had a bypass colostomy for persistent disease. Three of these locally advanced cases are alive without evidence of disease with intact canals from two years to six years following treatment. Thirty-seven of the 40 patients were treated with external beam radiation therapy alone using pelvic and/or perineal fields only. Three patients underwent interstitial implant. External beam radiation therapy doses varied from 4,500 rads to 7,000 rads (median, 6,700 rads) with standard fractionation of 180-225 rads 4-5 times a week over a total lapsed time of 5-8 weeks. The data suggest that there is a strong correlation with homosexuality. (no Refs)

33. COLORECTAL CANCER: RADIOTHERAPY.

Arnott SJ

Dept. Clinical Oncology, Western General Hosp., Univ. Edinburgh, Edinburgh EH4 2XU, England

Recent Results Cancer Res; 83:113-125 1982

The value of radiotherapy in the treatment of colorectal cancer is reviewed. While the concept of using a combination of drug therapy and radiation in the treatment of human tumors is attractive, it remains controversial. Some studies have indicated an improvement in results from combined regimens over those obtained with radiotherapy alone, but others have argued that it might have been possible to attain the same improvement in results by giving a higher dose of radiotherapy. It is generally believed that for most human tumors, radiation and cytotoxic drugs act in an additive rather than a synergistic fashion. A combined regimen of 5-fluorouracil plus radiotherapy, or radiotherapy alone, has been used in 325 patients treated at Edinburgh. Most of those with inoperable cancers gained significant relief of pain and mucoid rectal discharge. The complete eradication of local tumor masses, however, was achieved in only a few. For those patients suitable for radical radiotherapy the response rates achieved were much better. Dose levels in the order of 55 Gray in 20 fractions in a period of 4 wk was required for effective therapy in patients with inoperable or recurrent rectal carcinomas. In patients with inoperable rectal tumors, this form of treatment achieved a local tumor control rate of over 30%. Similar response rates were seen in patients with recurrent tumor after previous definitive surgical operation. Similar encouraging 5-yr-survival rates have been reported for other series in which patients with inoperable rectal carcinoma have been treated by radiotherapy. Patient selection, high dose radiotherapy studies, contact radiotherapy and interstitial techniques, developments in radiotherapy, and combined surgery and radiotherapy are also discussed. (22 Refs)

34. PHASE I AND PHARMACOLOGY STUDY OF ACIVICIN BY 24-HOUR CONTINUOUS INFUSION.

Weiss GR, McGovren JP, Schade D, Kufe DW

(c/o Kufe), Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115

Cancer Res; 42(9):3892-3895 1982

A Phase I trial of acivicin [L-(alphaS,5S)-alpha-amino-3-chloro-4,5-dihydro-5 isoxazoleacetic acid] has been performed on an escalating-dosage 24-hr continuous iv infusion schedule. Thirty-one patients received 77 courses of treatment, and all but one were evaluable for toxicity. Pharmacological monitoring in selected patients demonstrated that peak plasma levels correlated with dose. Postinfusion t1/2beta was 6 to 9 hr, and urinary recovery of the administered dose was 14 to 19% as unchanged drug during the 24-hr infusion. Hematological and gastrointestinal toxicities were variable and not dose related. In contrast, neurotoxicity characterized by lethargy, fatigue, confusion, disorientation, hallucinations, nightmares, and truncal ataxia was dose limiting and related to plasma drug levels. A minimal antitumor response was observed in a patient with colorectal carcinoma, and a partial response occurred in a patient with liver metastases from gastric carcinoma. The recommended dose for Phase II trial by 24-hr infusion is 160 mg/sq m. (Author abstract) (15 Refs)

35. IMPROVED REGIONAL SELECTIVITY OF HEPATIC ARTERIAL BCNU WITH DEGRADABLE MICROSPHERES.

Dakhil S, Ensminger W, Cho K, Niederhuber J, Doan K, Wheeler R (c/o Ensminger) Burroughs Wellcome Scholar in Clinical Pharmacology, Clinical Res. Center, Univ. Michigan Hosp., W4543, Box 055, 1405 E. Ann St., Ann Arbor, MI, 48109
Cancer; 50(4):631-635 1982

Starch microspheres 40 um in diameter, which are rapidly degraded by serum amylase, have been administered through hepatic arterial catheters to five patients with primary and metastatic liver cancer to determine whether (1) arterial blood flow through the liver could be temporarily blocked, and (2) such occlusion at the level of the arteriolar capillary bed would enhance regional uptake and catabolism and decrease systemic exposure to simultaneously administered hepatic arterial bischlorethylnitrosourea (BCNU). It was possible with 10 ml of microspheres (9 x 10(6) microspheres/ml) injected into the hepatic artery to transiently (for 15-30 min) reduce hepatic flow by 80-100% in the five patients. When BCNU (50 mg/m2 in 1 min) was given with microspheres there was a 30-90% reduction in systemic nitrosourea exposure and in peak levels. No myelosuppression was noted and hepatic toxicity consisted of acute pain due to BCNU and 1.5-2.0 fold transient enzyme elevations. One patient with cholangiocarcinoma showed a partial response lasting 3 mo; three patients had stable disease and one patient with colon carcinoma had progressive disease. Thus, this pilot study suggests that concurrent intra-arterial microspheres and BCNU may have the potential to improve selective regional drug effect with marked diminution in systemic toxicity. (Author abstract) (14 Refs)

36. LOCAL RECURRENCE AND HEPATIC METASTASES AFTER CURATIVE COLORECTAL SURGERY: IMPLICATIONS FOR ADJUVANT CHEMOTHERAPY (MEETING ABSTRACT).

Gilbert JM, Jeffrey I, Kark AE
Department of Surgery, Clinical Research Center, Watford Road, Harrow, England
British Association of Surgical Oncology Summer Meeting, July 15-16, 1982, Portsmouth, England British Association of Surgical Oncology; 1982

Adjuvant chemotherapy of colorectal cancer (CRC) aims to treat minimal residual disease following 'curative' surgery. Despite such treatment, a proportion of patients receiving adjuvant chemotherapy will subsequently develop recurrent tumor. We have identified the sites at which tumor recurs at necropsy in order to define more precisely how adjuvant chemotherapy should be directed. Six hundred and fifty necropsies with CRC from two hospitals were reviewed. Forty-five of these would have been suitable for adjuvant chemotherapy, ie, had a 'curative' operation and survived the perioperative period (four months), but subsequently died with recurrent tumor. Of these 45, 33 had recurrence in two or more places and in 12 it was confined to a single site. In these 12 the distribution of metastases was eight local, three hepatic and one pulmonary. When all 45 cases are considered together, the distribution was local 30, hepatic 21, peritoneal 18, lymph nodes 15 and pulmonary 12. It is concluded that disseminated disease is commonest and that local recurrence is more common than hepatic metastases. In patients suitable for adjuvant therapy, hepatic metastases have been considered the most important problem and treatment directed to them, but our findings suggest that hepatic metastases rarely occur in isolation. Therefore, adjuvant treatments should be directed both locally as well as systemically rather than solely at the liver. (no Refs)

37. THE TREATMENT OF HEPATIC METASTASES: INDICATIONS AND RESULTS.

Egeli RA, Balser S, Rohner A

Clinique de chirurgie digestive, Hopital cantonal universitaire, 1211 Geneva 4, Switzerland

Rev Med Suisse Romande; 102(4):389-397 1982

Of 83 hepatectomies, 26 (31%) involved hepatic metastases from a solid tumor. In 4/5 cases the site of the primary tumor was the colon or the rectum. In 8/21 cases, metastases were discovered during surgical intervention for the primary tumor. Adjuvant therapy included presurgical chemotherapy (3 cases), pre- and postsurgical chemotherapy (2), and postsurgical chemotherapy (4). Three patients died from surgical complications. The av postoperative survival rate was 16.8 mo excluding the three postsurgical deaths. One patient was alive at more than 6 yr after the surgery having undergone right hepatectomy for a very large tumor of the liver and enucleation of an isolated lesion of the left lobe. Another patient who underwent two separate procedures on each lobe for a carcinoid syndrome was asymptomatic and alive at 9 yr postoperatively. Based on the above results and an analysis of the literature, it is suggested that surgical resection of hepatic metastases is justified and may in some cases improve survival rates or provide substantial palliative benefits. (14 Refs) (In FRE)

38. LEVAMISOLE: A DOUBLE BLIND IMMUNOLOGICAL STUDY.

Webster DJ, Whitehead RH, Richardsn G, Hughes LE

Univ. Dept. Surgery, Welsh Natl. Sch. Medicine, Heath Park, Cardiff CF4 4XN, Wales

Anticancer Res; 2(1/2):29-32 1982

The immunological effects of levamisole (LV) were assessed in a randomized 4-wk trial in cancer patients with poor prognosis, who received active or inactive tablets. The study group comprised 68 patients (30 males, 38 females). Placebo was given to 32 of the patients with (stomach 10, colon 10, melanoma 12) while 36 patients with (stomach 9, colon 13, melanoma 14) received LV (150 mg/day 3x/wk). During 6 mo of follow-up there was no change in immunological status using a battery of tests which included dinitrochlorobenzene (DNCB) and Mantoux responses, lymphocyte count, phytohemagglutinin stimulation, and serum immunoglobulin levels. In the LV group, 16/36 patients complained of side effects which included nausea, vertigo, sweating, general malaise, abdominal pain and skin rash. Treatment was stopped in 17% of the patients. It is concluded that any beneficial effect of LV in patients with advanced cancer may be mediated by a non-immunological mechanism, or by some immunological process other then ones studied, or which may require a longer period of treatment than 4 wk. The variability of responses to DNCB seen in this study evaluated by a single observer in a double blind study suggests that results in open studies, or with different observers, must be interpreted with caution. (26 Refs)

OTHER CLINICAL AND PRE-CLINICAL ASPECTS OF COLORECTAL NEOPLASMS

39. CANCER OF THE COLON AND RECTUM IN HIGH-RISK PATIENTS.

Thompson JS, Pearlman N
Dept. Surgery, Univ. Nebraska Medical Center, 42nd and Dewey, Omaha, NE, 68105
Dis Colon Rectum; 25(5):461-463 1982

The experience with colorectal cancer at the Denver Veterans Administration Hospital was retrospectively reviewed to characterize the high-risk population with this disease and to determine what impact, if any, screening high-risk patients might have on overall survival rates. The high-risk patients comprised 12% of the overall population with colorectal cancer and did not differ from the latter in terms of age of onset, distribution of tumors, type of symptoms at diagnosis, or survival with a given stage of disease. They did, however, have more Stage A and B lesions and a better overall survival than did the general population with colorectal cancer, as a result of screening. The findings suggest that surveillance of high-risk groups is beneficial. Until ways are found to increase the number of patients eligible for inclusion in this group, however, these benefits are unlikely to lead to improved survival of the general population with colorectal cancer. (Author abstract) (24 Refs)

40. WHAT IS THE DUKES' SYSTEM FOR CARCINOMA OF THE RECTUM?

Fitzgerald RH
Dept. Radiation Therapy, Medical Univ. South Carolina, 171 Ashley Ave., Charleston, SC, 29403
Dis Colon Rectum; 25(5):474-477 1982

Analysis is made of the evolution of the currently used Dukes' system for post-surgical staging of carcinoma of the rectum. It is concluded that no further modification is likely to improve understanding of a patient's disease or prognosis. (Author abstract) (12 Refs)

41. COLORECTAL CANCER: PATHOLOGY AND NATURAL HISTORY.

Talbot IC
Dept. Pathology, Univ. Leicester, Leicester LE2 YLX, England
Recent Results Cancer Res; 83:59-66 1982

The genesis of colorectal cancer is reviewed. Epidemiological studies indicate that adenocarcinoma is most common in populations in which adenomas are most frequent, and that within these populations the age incidence of adenomatous polyps parallel those of cancer. The cardinal feature of malignancy in epithelial tumors of the large bowel is the presence of neoplastic glands infiltrating the submucosa beneath an ulcerated surface lesion. The concept of intramucosal or in situ cancer is not applicable to the large intestine. Villous adenomas, frequently large, were found to contain focal carcinoma in 40.7% of cases, while malignancy was found in 4.8% of tubular adenomas and in 22.5% of intermediate lesions. When tumor has not infiltrated beyond the muscular coats of the colon (Stage A) the 5-yr-survival (5YS) is comparable to that of the control population (96%). The 5YS rate of patients with carcinoma infiltrating the adventitial or subserosal adipose tissue (Stage B) is 78%, and when there are lymph node metastases (Stage C) the 5YS rate falls to 31%. Gross morphology and prognosis, cause of death and pattern of tumor dissemination, pathogenesis of distant metastases (venous invasion), and venous invasion, Dukes' stage, and survival are also discussed. (15 Refs)

42. COLORECTAL CANCER: PROSPECTS IN MANAGEMENT.

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Dept. Clinical Oncology, Univ. Edinburgh Western General Hosp., Edinburgh EH4 2XU, England
Recent Results Cancer Res; 83:135-149 1982

The multidisciplinary approach to the management of colorectal cancer, pre- and post-operative radiotherapy, adjuvant cytotoxic chemotherapy, and immunotherapy are discussed. In rectal cancer, mobility has been demonstrated to be of major prognostic significance. In the Medical Research Council's trial of adjuvant radiotherapy for operable rectal cancer, 79% of patients with mobile lesions had curative excisions, as opposed to only 30% of patients with fixed cancers. Development of new methods for the early detection of colorectal cancer must be encouraged. (42 Refs)

43. RESECTION OF LUNG METASTASES IN LARGE BOWEL CANCER.

Hughes ES, McConchie IH, McDermott FT, Johnson WR, Price AB
Dept. Surgery, Monash Univ., Alfred Hosp., Commercial Road, Prahran, Victoria 3181, Australia
Br J Surg; 69(7):410-412 1982

A series of 14 patients had partial or, in one case, total excision of the lung for metastatic tumor originating in the large bowel. Two patients have survived long periods (6 yr and 12 yr) and are now apparently free of the disease. A third patient shows no recurrence after bilateral lobectomy 2 yr ago. Six of the remaining 11 patients developed isolated pulmonary metastases 5 yr and 4 mo to 11 yr and 4 mo after the original bowel resection. All six survived for 9 mo to 11 yr after pulmonary resection before succumbing to the disease. In all 11 patients who died, death was caused by systemic metastases in the brain, spinal cord or bone. (Author abstract) (10 Refs)

44. DIFFUSELY INFILTRATING TYPE OF COLONIC CARCINOMA: REPORT OF A CASE.

Ashida K, Iwakoshi K, Masamune O, Hirata I, Asada S, Ohshiba S, Kurokawa A
Second Dept. Internal Medicine, Osaka Medical Coll., 2-7 Daigakucho, Takatsuki-shi 569, Japan
I To Cho; 17(4):435-440 1982

A case of diffusely infiltrating-type colon carcinoma occurred in a 45-yr-old man presenting with left side flank pain and lumbago. Discovery of well-differentiated adenocarcinoma in specimens obtained during left nephrectomy from the left kidney, ureter, and lymph nodes led to examination of the colon. The primary tumor nest was discovered in the distal descending colon and part of the sigmoid colon. The tumor was resected. Examination of the resected intestinal tissue confirmed a diagnosis of diffusely infiltrating type primary colon carcinoma, an extremely rare disease. (9 Refs) (In JPN)

45. PRIMARY SQUAMOUS-CELL CARCINOMA OF THE CECUM AND ASCENDING COLON. REPORT OF A CASE AND REVIEW OF THE LITERATURE.

Pittella JE, Torres AV
Dept. Pathology, Federal Univ. Minas Gerais Medical Sch., 30000 Belo Horizonte, Brazil
Dis Colon Rectum; 25(5):483-487 1982

A case of primary squamous-cell carcinoma at the cecum-ascending colon junction is reported as the 17th in world medical literature. Previous reported cases are reviewed and comments on their histogenesis and relationship with adenocarcinoma of the colon are presented. (Author abstract) (35 Refs)

46. SQUAMOUS EPITHELIAL CARCINOMA IN A SIGMOID DIVERTICULUM: CASE REPORT AND LITERATURE REVIEW.

Blessing H, Baltisser I
Chirurgische Klinik, Thurgauisches Kantonsspital, CH-8596 Munsterlingen, Switzerland
Chirurg; 53(6):377-381 1982

Squamous cell carcinoma in a sigmoid diverticulum is reported in a 72-yr-old woman. The patient presented with increasing irregularity of stool and loss of wt. Radiological studies showed a probably inflammatory stenosis of the rectosigmoid. A low anterior resection was performed with an end-to-end anastomosis and a temporary colostomy. The patient was free of pain and recurrence 24 mo after surgery. This case is the first of its type in the literature. (27 Refs) (In GER)

47. EPIDERMOID CARCINOMA OF THE ANUS WITH SECONDARY LUETIC INFECTION.

Schuman ES, Sullivan ES, Kimbrough RC
2228 N.W. Pettygrove St., Portland, OR, 97210
Am J Proctol Gastroenterol Colon Rectal; 33(7):6-7,20 1982

This patient is presented for two reasons. First, the unusual association of a perianal cancer with syphilis infection within the cancer. Second, for the successful application of radiation therapy. Numerous reports in the past have presented patients with genital syphilis associated with cancers in other portions of the body. What is unusual in this case is the simultaneous cancer and luetic infection occurring in the same location. The Darkfield examination is a relatively easy test to perform and is recommended in patients with perianal lesions who are sexually active. The present day application of high-dose super voltage radiation has more efficacy in this lesion than did the low-dose orthovoltage treatments of yr past. Most reports which have been unfavorable for irradiation have used the latter treatment. The use of this radiation therapy as a preoperative regimen can significantly decrease the extent of resection required in many cases and occasionally, as in this case, can be curative. It may be that radiation therapy alone or in a multimodality regimen is optimum for epidermoid carcinomas of the perianal region and further investigation of this is warranted. (Author abstract) (15 Refs)

48. NON-DYSPLASTIC VILLOUS CHANGES IN ENDOSCOPIC BIOPSIES IN ULCERATIVE COLITIS WITH CARCINOMA.

Rubio CA, Nylander G, Johansson C, Slezak P
Dept. Pathology, Karolinska sjukhuset, Box 60500, S-104 01 Stockholm, Sweden
Acta Pathol Microbiol Immunol Scand [A]; 90(4):277-282 1982

Three cases of long-standing ulcerative colitis and invasive adenocarcinoma are described. In all three cases, pre-operative rectal and/or colonoscopic biopsies demonstrated the presence of a villous adenoma: two without dysplasia and the third with moderate dysplasia. The presence of structures compatible with villous adenoma should be, even in the absence of epithelial dysplasia, an indication for panproctocolectomy in patients with long-standing ulcerative colitis. (Author abstract) (13 Refs)

49. CANCER COMPLICATING DEFUNCTIONED CROHN'S DISEASE.

Victor DW, Thompson H, Allan RN, Alexander-Williams J
Gastroenterology Unit, General Hosp., Steelhouse Lane, Birmingham B4 6NH, England
Clin Oncol; 8(2):163-165 1982

A case of adenocarcinoma developed in a rectal stump, defunctioned for 23 yr after total colectomy for Crohn's colitis. It escaped detection despite surveillance. In a series of 513 patients with Crohn's disease two other cancers have been detected in bypassed small bowel. It may not be the loop itself that causes the cancer, but the presence of the loop may hade chronic disease in situ for many years. (4 Refs)

50. EFFECTS OF CYCLOPHOSPHAMIDE AND POLYCYCLIC AROMATIC HYDROCARBONS ON CELL GROWTH AND MIXED-FUNCTION OXIDASE ACTIVITY IN A HUMAN COLON TUMOR CELL LINE.

Fang WF, Strobel HW
(c/o Strobel) Dept. Biochemistry and Molecular Biology, Univ. Texas Medical Sch. at Houston, Houston, TX, 77025
Cancer Res; 42(9):3676-3681 1982

Human Colon tumor cells (cell line LS174T) retain a cytochrome P-450-containing drug metabolism system capable of hydroxylating polycyclic hydrocarbons and the anticancer drug cyclophosphamide. The hydroxylation of benzo(a)pyrene by human colon tumor cells is highly inducible. Phenobarbital plus hydrocortisone induce benzo(a)pyrene hydroxylation activities 10-fold, while benz(a)anthracene induces the rate of hydroxylation 30-fold. Cytochrome P-450 specific content is increased two- to three-fold by treatment with phenobarbital plus hydrocortisone and benz(a)anthracene, respectively. Addition of cyclophosphamide alone results in no increase in hydroxylation activities but causes a decrease in cell growth rate. The combination of cyclophosphamide with either of the inducers phenobarbital plus hydrocortisone or benz(a)anthracene results in markedly enhanced inhibition of cell growth as judged both by a decrease in the number of cells per plate and in the incorporation of [3H]thymidine into DNA. Thus, these data show that cyclophosphamide is cytotoxic to human colon tumor cells and that the cytotoxicity is enhanced by simultaneous administration of benzo(a)anthracene or phenobarbital plus hydrocortisone to the tissue cultures. (Author abstract) (36 Refs)

51. ASSOCIATION OF CELL LETHALITY WITH INCORPORATION OF 5-FLUOROURACIL AND 5-FLUOROURIDINE INTO NUCLEAR RNA IN HUMAN COLON CARCINOMA CELLS IN CULTURE.

Glazer RI, Lloyd LS
NCI, Building 37, Room 6D28, Bethesda, MD, 20205
Mol Pharmacol; 21(2):468-473 1982

Cytocidal activity of 5-fluorouracil (5-FU) and 5-fluorouridine (5-FUR) was examined by soft agar cloning and the relation of the effects to nucleic acid synthesis and drug incorporation into nuclear RNA was investigated in a human colon carcinoma cell line (HT-29). After 2 hr of drug exposure, 5-FU was toxic only at 10(-3) M whereas almost a 2-log reduction in colony formation was achieved by 10(-5) M 5-FUR. Following a 2-hr or 24-hr exposure to 5-FU and 5-FUR, RNA and DNA syntheses were inhibited in a concentration-dependent manner. The synthesis of low mol wt (4 S) nuclear RNA was not significantly affected by treatment with either drug. No significant difference with the processing of ribosomal RNA (rRNA) was found by long- and short-term exposure to 5-FU and 5-FUR as assessed by lack of accumulation of rRNA greater than 28 S and by inhibition of formation of 28 S and 18 S rRNA. Measurements of the incorporation of [3H]5-FU and [3H]5-FUR into nuclear RNA by agarose gel electrophoresis indicated that 28 S and 18 S rRNA, as well as 4 S RNA, were the main RNA species labeled at noncytotoxic concentrations of drug. At cytocidal drug concentrations, 5-to 10-fold more [3H]5-FU or [3H]5-FUR was incorporated into nuclear 4 S RNA than rRNA. Results indicated that the primary determinant of cell lethality in HT-29 cells is the degree of fluoropyrimidine substitution in nuclear RNA and not inhibition of either DNA or RNA synthesis. (31 Refs)

52. CLONAL EVOLUTION DEMONSTRATED BY FLOW CYTOMETRIC DNA ANALYSIS OF A HUMAN COLONIC CARCINOMA GROWN IN NUDE MICE.

Vindelov LL, Spang-Thomsen M, Visfeldt J, Povlsen CO, Jensen G, Nissen NI
Dept. Internal Medicine, Finsen Inst., 49 Strandboulevarden, DK-2100 Copenhagen, Denmark
Exp Cell Biol; 50(4):216-221 1982

A spontaneous change in DNA content of a human colonic carcinoma grown in nude mice was observed fortuitously. The tumor initially had a G1 cell DNA content of 1.3x that of normal cells. Flow cytometric DNA analysis showed in transplant generation 56 the appearance of a new subpopulation which in three passages completely overgrew the original population. The DNA content of the new subpopulation was twice that of the original population. The observation supports the hypothesis of clonal evolution of tumor cell populations. The growth rates of the tumor before and after the change showed no significant difference (p greater than 0.05). Cell kinetic factors, therefore, offer no obvious explanation of how the overgrowth took place. It is not known whether the original population disappeared completely or survived as a small population below the detection limit. The heterogeneity created by clonal evolution of a tumor would be less pronounced if old subpopulations often become extinct as new ones emerge. Heterogeneity of human tumors is of clinical importance because the individual subpopulations may have different sensitivity patterns to antineoplastic drugs. (Author abstract) (14 Refs)

53. GROWTH STATE-SPECIFIC RESPONSIVENESS OF PRIMARY CULTURES OF A NUDE MOUSE-XENOGRAFTED HUMAN COLON CARCINOMA TO 4'-DEOXYDOXORUBICIN AND A CRUDE HUMAN LEUKOCYTE ALPHA-INTERFERON PREPARATION.

van der Bosch J, Zirvi KA
Diabetes Forschungsinstitutr, Auf'm Hennenkamp 65, 4000 Dusseldorf, W. Germany
Cancer Res; 42(9):3789-3792 1982

Improved procedures for the seeding of primary cultures from human colon tumors are described. Responsiveness of primary cultures from human colon carcinoma T348 to a crude preparation of human leukocyte alpha-interferon and a DNA-intercalating experimental anticancer drug, 4'-deoxydoxorubicin, has been investigated. The effect of the interferon preparation on such cultures is shown to be growth state specific; ie, stationary populations are killed, whereas fast-growing cultures are reversibly growth inhibited by the same doses of interferon. In contrast, 4'deoxydoxorubicin kills growing populations, whereas stationary cultures are barely affected by the same concentration of this drug. Interferon antagonizes the cytotoxic effect of 4'deoxydoxorubicin on a growing colon tumor cell population when applied immediately after 4'-deoxydoxorubicin treatment. Implications of this finding for the combined application of several drugs in cancer therapy are discussed. (Author abstract) (11 Refs)

54. ANTITUMOR EFFECT OF 3-[(4-AMINO-2-METHYL-5-PYRIMIDINYL)METHYL]-1-(2 CHLOROETHYL)-1-NITROSOUREA (ACNU) ON HUMAN COLON CARCINOMAS TRANSPLANTED INTO NUDE MICE.

Kubota T, Hanatani Y, Tsuyuki K, Nakada M, Asanuma F, Okazaki M, Ishibiki K, Abe O, Nakajima E, Maruyama K
Dept. Surgery, Kitasato Inst. Hosp., 9-1, Shirokane 5-chome, Minato-ku, Tokyo 108, Japan
Jpn J Clin Oncol; 12(1):33-41 1982

Effects of 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2 chloroethyl)-1-nitrosourea (ACNU) were studied in two human colon carcinomas (Co-3, well-differentiated adenocarcinoma; and Co-4, poorly-differentiated adenocarcinoma) serially transplanted into the backs of BALB/c male nude mice. Tumor size was measured 3x/wk and treatment, consisting of ACNU (20 and 40 mg/kg body wt) administered iv 1x, was initiated when the tumor wt was estimated to be 100-300 mg. Slight retardation, but no regression, of Co-3 tumor growth was observed after administration of 40 mg/kg of the ACNU. Regression of the Co-4 tumors was observed in mice treated with either 20 or 40 mg/kg. A dose response effect was observed, and Co-4 tumors regressed to almost half the wt of the initial tumors. Histologically, the treated Co-4 tumors showed marked decrease in cell population, swollen destroyed tumor cells, and massive fibrosis around the tumor cells. Microangiograms of both types of tumors revealed hypervascular features similar to human adenocarcinomas of the colon. Whole-body autoradiography using [ethylene-2-14C]-ACNU showed a peak ACNU concentration 30 min after injection in the Co-3 tumor, but the ACNU was retained in the Co-4 tumor up to 360 min after injection. The antitumor effects of the ACNU were thought to be correlated with the concentration of the drug in the tumor. (21 Refs)

55. IN VITRO RESPONSES OF NUDE MOUSE-XENOGRAFTED HUMAN COLON CARCINOMAS EXPOSED TO DOXORUBICIN DERIVATES IN TISSUE CULTURE AND IN THE MOUSE.

Zirvi KA, Van der Bosch J, Kaplan NO
Dept. Chemistry, Vanderbilt Univ., Box 1822. Station B, Nashville, TN, 37235
Cancer Res; 42(9):3793-3797 1982

In vitro responses of four xenografted human colon tumors (T183, T219, T245, and T348) to various doses of 1'-deoxydoxorubicin have been investigated. The individual tumors showed marked differences in drug responsiveness, ranging from high sensitivity at low doses (T219; 125 ng/ml) to very low sensitivity at high doses (T245; 4,000 ng/ml). The sensitivity ranking deduced from these in vitro experiments correlates well with the ranking deduced earlier from in vivo drug treatments of transplants of these tumors in the nude mouse. The effect of in vitro drug treatment (4'-deoxydoxorubicin; 250 ng/ml; 1-hr incubation) on the in vivo growth of one of the tumors, T219, in nude mice was investigated. Growth of the tumor in nude mice was markedly delayed by pretreatments in vitro with 4'-deoxydoxorubicin. Furthermore, in vitro responsiveness of the T219 tumor was investigated following in vivo and in vitro treatment of the tumor with 4'-deoxydoxorubicin. Both of the pretreatments produced very similar decreases in drug responsiveness to all of the doxorubicin derivatives tested 4'-deoxydoxorubicin, 4'-O-methyldoxorubicin, 4'-epidoxorubicin, 4'-demethoxydoxorubicin, and N-trifluoroacetylodoxorubicin-14-valeriate. (Author abstract) (12 Refs)

56. IN VIVO-IN VITRO CLONOGENIC ASSAYS IN A HUMAN TUMOUR XENOGRAFT WITH A HIGH PLATING EFFICIENCY.

Warenius HM, Bleehen NM

Regional Radiotherapy Centre, Newcastle General Hosp., Westgate Road, Newcastle Upon Tyne, England

Br J Cancer; 46(1):45-50 1982

The HT29R human colonic adenocarcinoma cell line grows as locally invasive, mucin-secreting tumors in immunosuppressed mice with a doubling time of 6 days. These tumors may be disaggregated to give single-cell suspensions with plating efficiencies of 25-45% in technically simple in vivo-in vitro cell-survival assays. The effect of maximum tolerated doses of 5-fluorouracil, melphalan and cyclophosphamide on in situ growth is only slight. In vivo-in vitro cell-survival assays are consistent with these in situ results. The relative ease of experimental manipulation and the high clonogenic efficiency of this tumor make it a useful addition to human tumor xenograft models. (Author abstract) (7 Refs)

57. DETECTION OF HUMAN CANCER IN AN ANIMAL MODEL USING RADIO-LABELED TUMOUR-ASSOCIATED MONOCLONAL ANTIBODIES.

Epenetos AA, Nimmon CC, Arklie J, Elliott AT, Hawkins LA, Knowles RW, Britton KE, Bodmer WF

Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England

Br J Cancer; 46(1):1-8 1982

Monoclonal antibodies to epithelial-cell antigenic determinants, labeled with 123I and 125I, were administered parenterally to immunodeficient mice bearing human tumors derived from a human cancer cell line. Anterior, posterior and lateral radioscans of the body were taken with a gamma scintillation camera at various times from immediately to 65 days after injection. Visual displays of the images were processed by standard computer techniques. The model used a human colon-cancer cell line, HT29, and the monoclonal antibody, AUA1, which is specific to an epithelial proliferating antigen. Tumor detection was achieved in all the mice. The smallest tumor detectable appeared to be about 1 mm in diameter. The degree of antibody uptake in a tumor depended on its size and the blood supply of its surrounding tissues. We believe that the technology and skills are now available for accurate radioimmunodetection of cancer in man. (Author abstract) (23 Refs)

58. COMPARATIVE GROWTH OF HUMAN TUMORS IN PHARMACOLOGICALLY IMMUNOSUPPRESSED, IMMUNE-DEPRIVED, CYCLOSPORIN A-TREATED AND NUDE MICE.

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Eur J Cancer Clin Oncol; 18(6):589-594 1982

The growth of three human tumor xenografts, namely on Ewing sarcoma, a colon carcinoma and an osteosarcoma, was compared in nude and conditioned mice. Conditioning protocols included (1) immune deprivation (thymectomy, lethal irradiation and cytosine arabinoside pretreatment); (2) immunosuppression with procarbazine, cyclophosphamide and antithymocyte serum; and (3) continuous administration of cyclosporin A. Similar tumor growth was seen in nude mice, immune-deprived mice and mice treated with the medium and high-dose immunosuppressive protocol. Cyclosporin A allowed only very modest tumor growth. In the main comparative experiment with the Ewing sarcoma and the colon carcinoma, overall survival was lowest with nude mice (17%), higher with immune-deprived mice (61%) and best with immunosuppressed mice (81 and 87%). For the screening of anticancer agents the immunosuppressive protocol consisting of synergistic procarbazine, cyclophosphamide and antithymocyte serum may be added to the already available models. It allows adequate tumor growth with good animal survival and does not require operative procedures and irradiation. (Author abstract) (16 Refs)

59. EFFECTS OF HIGH-DOSE AND LOW-DOSE PREOPERATIVE IRRADIATION ON LOW ANTERIOR ANASTOMOSES IN DOGS.

Bubrick MP, Rolfsmeyer ES, Schauer RM, Feeney DA, Johnston GR, Strom RL, Hitchcock CR

Dept. Surgery, Hennepin County Medical Center, 701 Park Ave., Minneapolis, MN, 55415

Dis Colon Rectum; 25(5):406-415 1982

Twenty mongrel dogs underwent preoperative irradiation to the colon and rectum, receiving 4,000 rads according to the Nominal Standard Dose Equation. Each dog then underwent anterior resection of the rectosigmoid, and reconstructive technique was randomized into two groups consisting of either hand sewn or EEA-stapled anastomoses. Anastomoses were examined digitally and radiographically at the time of surgery and on the 7th postoperative day. There were four radiographic leaks among the hand sewn anastomoses, but only one was clinically significant and associated with peritonitis. There were no leaks among the 10 EEA-stapled anastomoses. The data suggest that low anterior resection and anastomosis can be done safely after 4,000 rad irradiation and that the EEA-stapled anastomosis may be preferable. (Author abstract) (25 Refs)

60. EFFECTS OF LOW-DOSE PREOPERATIVE IRRADIATION ON LOW ANTERIOR ANASTOMOSIS IN DOGS.

Schauer RM, Bubrick MP, Feeney DA, Johnston GR, Rolfsmeyer ES, Strom RL, Hitchcock CR

(c/o M. P. Bubrick) Dept. Surgery, Hennepin County Medical Center, 701 Park Ave. South, Minneapolis, MN, 55415

Dis Colon Rectum; 25(5):401-405 1982

Twenty mongrel dogs underwent preoperative radiation therapy to the colon and rectum using the Nominal Standard

Dose Equation to simulate treatment with 2,000 rad. Each dog then underwent anterior resection of the rectosigmoid, and reconstruction was randomized into two groups consisting of either hand sewn or EEA-stapled anastomoses. Anastomoses were examined digitally and radiographically on the day of surgery and on the 7th postoperative day. There were three radiographic leaks among the 10 dogs having the hand sewn anastomoses and one radiographic leak among the 10 dogs having the EEA-stapled anastomoses. There was one clinically significant leak which occurred in a dog having an EEA-stapled anastomosis and was associated with peritonitis and death. The overall leak rate was 30% among dogs having hand sewn anastomoses and 20% among dogs with stapled anastomoses. The data suggest that an anterior resection in low colorectal anastomosis can be done safely after low-dose radiation using either hand sewn or stapling techniques. (Author abstract) (19 Refs)

61. COLORECTAL CANCER: CELL KINETICS.

Camplejohn RS
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Recent Results Cancer Res; 83:21-30 1982

Dynamic changes occurring within epithelial cell compartments in both normal and transformed colorectal tissue are discussed. The proliferative compartment of normal colonic mucosa, ie, that zone of cells in which replication takes place, is limited to the lower two-thirds of crypts under normal conditions, but expands to include every level of the mucosa during the transformation process. Mathematical descriptions of the cell cycle as it applies to colonic mucosa in both the normal and diseased states are given. Colorectal carcinomas generally grow slowly. Cell production by mitosis in these tumors is not increased compared with that in histologically normal mucosa. Growth of these tumors is due to a small decrease in cell loss rather than an increased rate of cell proliferation. Growth curve and doubling time data, fraction of labelled mitosis technique, stathmokinetic technique, comparison of growth curve, fraction of labelled mitosis, and stathmokinetic results, and tumor heterogeneity are also discussed. (28 Refs)

62. HIGH-DENSITY LIPOPROTEINS AND THE PROLIFERATION OF HUMAN TUMOR CELLS MAINTAINED ON EXTRACELLULAR MATRIX-COATED DISHES AND EXPOSED TO DEFINED MEDIUM.

Gospodarowicz D, Lui GM, Gonzalez R
Cancer Res. Inst., Univ. California Medical Center, San Francisco, CA, 94143
Cancer Res; 42(9):3704-3713 1982

The ability of high-density lipoprotein (HDL) to support the growth of an established tumor cell line exposed to defined medium supplemented with transferrin has been examined. Low-density A-431 carcinoma cells maintained on extracellular matrix- or fibronectin-coated dishes proliferated actively when exposed to a synthetic medium supplemented with HDL, 500 ug protein per ml. Epidermal growth factor added at concentrations above 0.5 ng/ml inhibited cell growth, while at concentrations above 5 ng/ml it was cytotoxic. Among the various substrata tested for their ability to support the active proliferation of low-density A-431 cells when exposed to transferrin and HDL, plastic was the least efficient. On fibronectin-coated dishes, cells ceased to proliferate after 8 population doublings, while on extracellular matrix-coated dishes cells could be passaged for 50 population doublings. In the case of colon carcinoma, rhabdomyosarcoma, and Ewing's sarcoma cells exposed to medium supplemented with transferrin, the addition to the cultures of HDL alone resulted in a growth rate and final cell density which were similar to those observed when cells were exposed to serum-supplemented medium. In the case of the mammary carcinoma cell lines MCF-7 and ZR-75-1, HDL also supported cell growth, although to a lesser extent than did serum. The present study therefore indicates that HDL is capable of supporting, either totally or partially, the in vitro proliferation of tumor cells. (Author abstract) (39 Refs)

63. DIFFERENCES IN METABOLISM OF CHEMICAL CARCINOGENS IN CULTURED HUMAN EPITHELIAL TISSUES AND CELLS.

Harris CC, TrumpBF, Grafstrom R, Autrup H
Lab. Human Carcinogenesis, NCI, NIH, Bethesda, MD, 20205
J Cell Biochem; 18(3):285-294 1982

Activation and deactivation of chemical procarcinogens were studied in cultured, nontumorous human epithelial tissues and cells. Procarcinogens were selected primarily on the basis that they represented several chemical classes and were found in the diet, drinking water, polluted air, and/or tobacco smoke. Conversion of the procarcinogens by cultured human tissues into metabolite(s) that bind covalently to DNA was investigated. Cultured human bronchus converted every procarcinogen studied into forms that bind to DNA. Carcinogens, such as aflatoxin B1, were activated to carcinogen-DNA adducts by cultured human tissues, bronchus, esophagus, colon, and bladder, even though epidemiological studies have not implicated aflatoxin B1 as a cause of cancer at these tissues. Metabolism of benzo[a]pyrene (BAP) and formation of DNA adducts were studied in cultured human tissues collected at the time of immediate autopsy. BAP metabolism and DNA binding were highest in the bronchus. Results indicated that quantitative extrapolations of carcinogen binding data may be possible among some, but not all tissues, and when different chemical classes of carcinogens are compared, quantitative and predictive correlations may frequently not be observed. Differences in carcinogen metabolism among people may be qualitative and/or quantitative. The magnitude of the differences ranges from 50-to 150-fold and is similar to that found in pharmacogenetic studies of drug metabolism. The rate-limiting enzymatic reaction could differ among humans and tissue types. (60 Refs)

64. EFFECT OF BILE ACIDS ON 1,2-DIMETHYLHYDRAZINE-INDUCED COLON CANCER IN RATS.

Koga S, Kaibara N, Takeda R
Dept. Surgery, Tottori Univ. Sch. Medicine, Yonago-shi, Nishi-machi 36-1, Tottori 683, Japan
Cancer; 50(3):543-547 1982

The effects of intercepting a part of the enterohepatic circulation of bile acids by ileal resection or bypass on the quantitative and qualitative changes of fecal bile acids were investigated in rats, and the relationship of these changes to the development of DMH-induced colon cancer was studied. The daily fecal total bile acid level was increased in all intercepted groups, especially those with long resection and exclusion. Total bile acid levels played a greater role in the development of DMH-induced colon cancer than did primary or secondary bile acid levels individually. Our findings suggest that bile acid acts as a promoter in the development of colon cancer. (Author abstract) (19 Refs)

65. CARCINOGEN-INDUCED DNA DAMAGE AND CELLULAR ALTERATIONS IN F344 RAT COLON ORGAN CULTURES.

Telang NT, Williams GM
(c/o Williams) Div. Pathology and Toxicology, Naylor Dana Inst. Disease Prevention, American Health Foundation, Dana Road, Valhalla, NY, 10595
JNCI; 68(6):1015-1022 1982

Optimized culture conditions were used to achieve prolonged survival of colon mucosa from conventional inbred F344 strain rats. Up to 21 days in culture, a high percentage of explants had viable mucosa with intact crypt columns and maintained active replicative DNA synthesis in the proliferative zone of the crypts. An acute 4-hr in vitro exposure to 0.5 mM of the colon-selective carcinogens 1,2-dimethylhydrazine dihydrochloride (DMH) and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) produced 26 and 78% suppressions of replicative DNA synthesis, respectively, whereas the same exposure to the liver carcinogen dimethylnitrosamine produced only a 5% suppression. the thymidine-labeling index of DMH-exposed cells was lower than that of control cells at 1 day and then increased above the control values 7-21 days later. MNNG exposure produced pronounced morphologic changes in the crypt columns. MNNG-exposed cultures that were transplanted into the mammary fat pads of syngeneic female rats produced hypercellular cysts different from those formed by nonexposed fragments. These findings indicate that the acute and persistent effects of colon carcinogens can be studied directly on the target tissue in organ cultures. (Author abstract) (46 Refs)

66. STUDY OF KINETICS OF EPITHELIAL CELL POPULATIONS IN NORMAL TISSUES OF THE RAT'S INTESTINES AND IN CARCINOGENESIS. III. CHANGES IN KINETICS OF ENTEROCYTE POPULATIONS IN THE COURSE OF EXPERIMENTAL INTESTINAL TUMOUR INDUCTION IN RATS.

Pozharisski KM, Klimashevski VF, Gushchin VA
Lab. Experimental Tumours, N.N. Petrov Res. Inst. Oncology, 68 Leningradskaya St., Pesochny-2, Leningrad 188646, USSR
Exp Pathol; 21(3):165-179 1982

A stage-by-stage study of disturbances in enterocyte proliferation in the ileum and descending colon in the course of tumor induction by treatment with 1,2-dimethylhydrazine was performed. Even at early stages, an expansion of the zone of epithelial cell proliferation in the crypts and migration of dividing cells as far as to the crypt mouth, which is a manifestation of enterocyte differentiation disturbances, were observed. Enterocytes of the crypts chiefly proliferated through a short cycle, the mean duration of which was slightly greater than in normal intestinal tissue. The reduced cell loss in the epithelium and resultant disturbances of its steady state led to the accumulation of great numbers of atypical cells in the superficial layers of the crypts and formation of carcinomas in situ in the descending colon. The microscopically unaltered sections of the mucosa, prior to development of overt neoplastic changes carcinomas in situ, superficial cancers and small-size adenocarcinomas revealed a simplified structure of enterocyte population, as compared with normal epithelium. As tumors progressed, the heterogeneity of its component cell subpopulations increased, and several subpopulations, differing in mean duration of the mitotic cycle, were formed. Pathologic mitoses made up a greater portion (50-60%) of the dividing cells of the descending colon, as compared with ordinary 4% at all stages of experimental tumor induction. (Author abstract) (23 Refs)

67. STRAIN DIFFERENCES IN SUSCEPTIBILITY OF FEMALE MICE TO 1,2-DIMETHYLHYDRAZINE.

Turusov VS, Lanko NS, Krutovskikh VA, Parfenov YD
Cancer Res. Center, Kashirskoye shosse 6, 115478, Moscow, USSR
Carcinogenesis; 3(6):603-608 1982

C3H, CBA, C57Bl/6j, (CBA x C57Bl/6j)F1, BALB/c, DBA/2, C3HA and AKR female mice were treated with 25 weekly sc injections of a solution of 1,2-dimethylhydrazine (DMH) in water at a dose level of 8 mg/kg body weight. BALB/c mice appeared to be most sensitive to the induction of epithelial colorectal (93.3%) and anal tumors by DMH. There was, however, a dissociation between the severity of the macroscopical tumor lesions in the colon of BALB/c mice and their relatively weak tendency to infiltrative growth. C3HA mice were more resistant to the induction of intestinal tumors (30.9%) but the tumors showed a deep invasion into the intestinal wall. There was no correlation between the strains and within a given strain between the development of colorectal and anal neoplasms. C3H and CBA mice strains developed a high incidence of uterine sarcomas (37.5 and 40.7%, respectively) which were not found at all in BALB/c, DBA/2 and C3HA mice and which appeared in C57Bl/6j and AKR mice at low frequency (2.7 and 7.7%, respectively). C57Bl/6j, BALB/c, DBA/2 and C3HA mice developed hemorrhagic lesions of the ovaries, (35.1, 46.7, 62.9 and 85.7%, respectively). These lesions, which led to peritoneal hemorrhage, were one of the main causes of death in C3HA and DBA/2 strains. It seems that, with the exception of AKR mice, an inverse relationship exists between the occurrence of hemorrhagic ovarian lesions and development of uterine sarcomas in female mice treated with DMH. (Author abstract) (18 Refs)

68. THE PROLIFERATIVE EFFECT OF DIETARY BUTYLATED HYDROXYANISOLE ON METHYLAZOXYMETHANOL TREATED COLONIC MUCOSA.

Deschner EE, Wattenberg LW
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Lett; 16(2):197-202 1982

Ability of butylated hydroxyanisole (BHA) to affect colonic epithelial cell proliferation and thereby influence neoplastic expression was studied in female CF1 mice. Mice were separated into two groups, one receiving semi-synthetic diet without BHA added and the other, a diet containing BHA at concentration of 5 g/kg. After 1 wk of the diet, animals were injected with methylazoxymethanol acetate (MAMA, 0.4 mg/mouse) once a wk for 6 wk. Animals were killed 3, 4, and 7 days after the first injection and 1 wk after the last injection. One hr prior to death, 25 uCi of 3H-thymidine was injected. Examination 3 and 4 days after the first injection showed the labeling index (LI) in rodents not fed BHA to be 18.6 +-2.0 compared with 17.9 +-1.3 in the BHA supplemented group. Only a slightly greater percentage of DNA synthesizing cells occupied the lower third zone of the crypts of the MAMA group receiving dietary BHA and shift of the proliferative compartment to the middle and upper third was less than among animals treated with MAMA alone (17.3% vs 18.3%). One wk after the last MAMA injection, the animals receiving a diet with no BHA added had a LI of 11.4 +-1.7 while those on dietary BHA had a LI of 8.8 +-2.7. While the LI were not significantly different because of large inter-animal variability, the distribution of labeled cells was noticeably altered. The addition of BHA to the diet of MAMA treated mice did not prevent the extension of the proliferative compartment to the surface (Stage I abnormality), but did restrain the shift of DNA synthesis to the middle and upper third of the crypt producing only 18.5% labeling in the region as compared with 26.4% in the group not receiving BHA. (6 Refs)

SELECTED ASPECTS OF COLO-RECTAL CANCER ETIOLOGY, EPIDEMIOLOGY, AND CARCINOGENESIS

69. NEOPLASIA AND URETEROSIGMOIDOSTOMY: A COLONOSCOPY SURVEY.

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Br J Surg; 69(7):414-416 1982

Patients who have undergone implantation of ureters into the sigmoid colon (ureterosigmoidostomy) are known to be at high risk of developing cancer of the colon many yr later. The operation is often performed in infancy for congenital abnormalities of the bladder, thus creating a long term surveillance problem. Six of 34 patients (17.6%) who had undergone ureterosigmoidostomy were found at a screening fibersigmoidoscopy to have adenomas of the left colon or severe dysplasia of the stoma, a mean interval of 22 yr after their urinary diversion. Four other patients had previously had a sigmoid adenoma or cancer; thus, 29% overall had developed colonic neoplasms, almost all closely related to their stomas. Another patient who, by error, was excluded from the surveillance, died of metastatic cancer of the sigmoid colon within the study period. Regular surveillance by fibersigmoidoscopy of patients who have had urinary diversion affords the opportunity to detect and remove potentially malignant sigmoid lesions. In addition to its clinical importance, it allows a closer study of this unique model of colon carcinogenesis. (Author abstract) (15 Refs)

70. CANCER MORBIDITY IN ULCERATIVE COLITIS.

Prior P, Gyde SN, Macartney JC, Thompson H, Waterhouse JA, Allan RN
Gastroenterology Unit, General Hosp., Birmingham, England
Gut; 23(6):490-497 1982

Cancer morbidity at all sites has been studied in a series of 676 patients with ulcerative colitis under long-term review, of whom more than two-thirds had extensive disease, and the level and pattern of risk over time examined. Age-, sex-, and site-specific incidence rates were used to compute the number of cancers that might have been expected to occur. A highly significant excess of cancers was observed overall but the excess was due entirely to cancers of the digestive system. In women there was no excess or deficit of cancers outside the digestive system. In men there was a small deficit of cancers of the respiratory system. An overall 11-fold excess colorectal cancer risk was found in the series compared with that in a relevant general population after patient-years at risk had been corrected for surgical resection and patients with colorectal cancer at their first referral had been excluded. When these data were expressed in an actuarial form the cumulative probability of developing colorectal cancer in the series was 8% (3.5-13%) at 25 yr, after the diagnosis of ulcerative colitis had been established. The relative risk of developing colorectal cancer was highest in those patients developing colitis before the age of 30 yr, and the relative risk fell as the age at diagnosis of their colitis increased. The pattern of risk of colorectal cancer over time suggests that there is an association between cancer and colitis in susceptible individuals and that the level of risk is related to age at onset of colitis. (Author abstract) (16 Refs)

71. COLORECTAL CANCER: GENETIC FACTORS.

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Recent Results Cancer Res; 83:45-58 1982

Genetic factors associated with increased risk of colorectal cancer are illustrated using familial polyposis coli (FPC) as an example. Features of FPC include the presence of numerous adenomatous polyps, a high incidence of associated colorectal cancer, and a proven genetic origin. The adenomas seldom number less than 500 and may sometimes exceed 5,000. The av number in colectomy specimens is about 1,000, fairly evenly distributed around the colorectum. Polyps begin to appear by the age of 20 yr, with symptoms appearing about 10 yr later. Two-thirds of all patients presenting with symptoms are found to already have colorectal cancer. The only effective treatment is surgical removal of the whole large intestine, necessitating ileostomy, or by resection of the colon only. Rectal adenomas can be destroyed by diathermy. FPC provides a useful experimental model supporting the adenoma-carcinoma sequence, adenomas and carcinomas in polyposis and non-polyposis patients, the genetic origin of adenomas, colorectal cancer families, difficulties in determining the inheritance of adenomas, the relationship between genetic and environmental factors, and the prevention of colorectal cancer are also discussed. (21 Refs)

72. RELEVANCE OF COLONIC MUCOSAL INFLAMMATION TO AETIOLOGY.

Earnshaw P, Busuttil A, Ferguson A
Gastrointestinal Unit, Univ. Edinburgh, Edinburgh EH4 2XU, England
Recent Results Cancer Res; 83:31-44 1982

Clinical and epidemiological evidence indicating increased risk of colorectal cancer in patients with chronic inflammatory diseases of the intestine are reviewed, and experimental aspects of intestinal immunological reactions and their relevance to colorectal cancer are discussed. Chronic inflammatory diseases of the intestines that are associated with colorectal cancer risk include ulcerative colitis, Crohn's disease, coeliac disease, radiation-induced colitis, and Schistosomiasis. Although the clinical manifestations of amebiasis closely mimic idiopathic ulcerative colitis, there is no associated increased risk for colorectal cancer. There is no known association between chronic diverticular disease, or ischemic colitis, and carcinoma, even though diverticula in other organs are associated with increased risk of carcinoma, e.g., in the pharynx, esophagus, and bladder. Primary immunodeficiency disease is often complicated by malignancy, especially lymphoma, and also occasionally gastric carcinoma. Management policy for high-risk patients, immunological reactions and colonic inflammation in experimental animals, mucosal T cells and the gut-associated lymphoid tissue, effects of local immune reactions on intestinal mucosa, reaginic hypersensitivity, immune complex hypersensitivity, and T-cell mediated immune reactions are among other topics discussed. (43 Refs)

73. COLORECTAL CANCER: ETIOLOGY.

Kinlen LJ
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Recent Results Cancer Res; 83:11-20 1982

Genetic and environmental (dietary) factors associated with an increased risk of colorectal cancer are reviewed. Genetic factors include the gene for familial polyposis coli, carried by about 1/10,000 people. Dietary factors found to correlate with colorectal cancer incidence include beer, fruit and milk, meat, legumes, starches, fish, dairy products (except milk). The evidence is more consistent for a protective effect of vegetables than for a harmful effect of fat or meat. (40 Refs)

74. RECENT TRENDS IN CANCER INCIDENCE IN KIEV 1969-1979.

Gualitser LN, Matvilchuk YD
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Neoplasma; 29(2):129-134 1982

The analysis of the trends of age-adjusted incidence rates of malignant tumors in the city of Kiev in the yr 1969-79 revealed a gradual increase of the majority of individual sites, mainly of the malignant tumors of rectum, lymphoid and hematopoietic tissues in both sexes and of breast in females. On the other hand a decrease of incidence rates of the malignancies of skin, lip and stomach in both sexes and of esophagus, lung and uterine cervix in females was noted. These investigations formed the basis of the prognosis study of incidence rates of malignant tumors in Kiev until 1990. The importance of the study of incidence rates and trends of individual sites of malignant tumors for the investigation of their factors and causes in urban conditions and environment is emphasized. (Author abstract) (8 Refs)

75. PREDICTION OF THE FUTURE INCIDENCE OF CANCER IN JAPAN.

Shiraishi M, Arimoto H, Chiba S, Takano A, Sato Y, Shimamura K, Shiraishi M, Nagasaki M, Ueda A, Shimizu K, Tominaga S, Fujimoto I, Cho T, Irie K, Watanabe M, Takagi K, Wakabayashi T, Nishiuchi I, Shigematsu T, Ishibashi H, Ikeda T, Odo Y
Natl. Cancer Center, 1-1 Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Jpn J Clin Oncol; 12(1):65-71 1982

Future incidence of cancer was predicted with consideration of the trend in age-specific incidence rates and the structure of the future population of Japan. The future trend of age-specific incidence rates according to the main site in primary cases in each sex was determined based on cancer registries of Miyagi Prefecture, Osaka Prefecture, Hiroshima City, and Nagasaki City. Linear regression was applied to the data from each registry as time clustering for evaluation of incidence rates differed from registry to registry. The total number of new cancer patients was predicted to be 319,000 in 1990 and 453,000 in 2000; the proportion of new patients age 65 yr and over will increase to 62.1% in 1990 and 75.2% in 2000. The number of new patients with cancer of the stomach, colon, and lung will increase for both sexes; however, uterine cancer will decrease. Standardized incidence rates for stomach cancer in both sexes and uterine cancer show a tendency to decrease, while the rates for colon and lung cancer are increasing. The incidence rates for all cancers seem to be constant for males less than 35 yr old and females less than 25 yr old, show a tendency to decrease for males 35-69 yr old and females 25-74 yr old, and are increasing rapidly for males 70 yr old or older and females 75 yr old or older. Incidence rates of stomach, colon, lung, and uterine cancers each have specific trends depending upon age groupings. Prediction of future incidence is necessary for planning policies against cancer. (5 Refs)

76. THE EPIDEMIOLOGY OF CANCER IN CHINA.

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World Health Forum; 3(1):95-101 1982

Epidemiology of cancer in China based on a retrospective survey of cancer mortality with additional data on the main cancer sites is reviewed. A total of 18,439,072 deaths were surveyed and 1,868,310 (10.1-11.3% in males and 8.8% in females) were attributed to cancer. The highest level of diagnosis and treatment and the best available criterion for the diagnosis of cancer are summarized. For all sites of cancer together the estimated mortality rates in China were 119.6/100,000 for males and 80.7/100,000 for females, adjusted to age distribution of the 'world' population. Among countries reporting mortality by site of cancer, China has the highest mortality from esophageal cancer with annual rates of 31.7/10,000 in males and 15.9/100,000 in females. Cancer of the stomach is the most common form of cancer leading to death in China. The mortality rates are 32.4 and 15.9/100,000 in males and females, respectively. The rates are substantially lower than those in Japan. Liver cancer (presumed primary) is the third more important cancer as a cause of death in China and accounts for 15% of all cancer deaths. Mortality rates of the cancer of the cervix are generally higher in the rural than in urban areas. An unusual feature of the high rate of lung cancer in Chinese women, particularly Cantonese women, is the relatively high proportion of the tumors which are adenocarcinomas. The county with highest rates of large bowel cancer is an area of endemic schistosomiasis in Zhajiang province. The geographic distribution of nasopharyngeal cancer within China is quite remarkable, with a very high incidence area centered on Guandong province in the south. (11 Refs)

77. COLORECTAL CANCER: RECENT TRENDS.

Fraser P, Adelstein AM
Epidemiological Monitoring Unit, Sch. Hygiene and Tropical Medicine, London, England WC1E 7HT
Recent Results Cancer Res; 83:1-10 1982

Trends in the age, race, and sex distribution of incidence and mortality rates of colorectal cancer in various countries are reviewed. Geographic, ethnic, and regional differences in the distribution of these cancers were apparent. A higher risk is observed in urban populations, in lower social classes, with a greater mortality among males. Low rates of survival make prevention a cause to be vigorously pursued. (12 Refs)

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